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DISSEMINATED LUPUS ERYTHEMATOSUS.[1]

By RICHARD B. PERKINS,
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THERE is some confusion as to the meaning of the word "disseminated" when applied to *lupus erythematosus*, and a brief historical review may be helpful. The first to describe any form of *lupus erythematosus* was Biett, who in 1828 described as *erythème centrifuge* what we now call the chronic discoid form. The name *lupus erythematosus* was coined by Cazenave (1851). Kaposi in 1872 was the first to describe a fatal case of *lupus erythematosus*, which he did under the title of *erysipelas perstans faciei*. Kaposi (1875) was also the first to apply the word "disseminated" to the disease, when he wrote as follows:

> Lupus erythematosus may be . . . developed . . . secondly, as disseminated and aggregated small spots . . . which I call lupus erythematosus disseminatus et aggregatus. [In this form] . . . hundreds of spots of erythematous lupus become distributed over . . . almost the whole body . . . accompanied by various local and constitutional symptoms.

From this and other (1899) examples of the use of the word "disseminated" by Kaposi, it is evident that he was referring to cutaneous dissemination of the lesions. However, as he recognized, such patients may have constitutional symptoms, and some confusion has been caused by later authors writing of disseminated *lupus erythematosus* when referring to patients with severe constitutional symptoms irrespective of the presence of a rash and its distribution.

I feel that it would be clearer to restrict the word "disseminated" to indicate the presence of lesions scattered over the skin of the trunk and limbs, as it was used by Kaposi, and to use "systemic" when we mean that the viscera and reticulo-endothelial and hæmatopoietic systems are affected. This use of the word "systemic" was suggested by Arnold (1950) and has since been widely adopted.

Classification.

The classifications of *lupus erythematosus* are somewhat arbitrary, but I shall follow that of Michelson (1952). I shall deal mainly with the cutaneous lesions and leave the other aspects to Dr. Helen Taylor.

Acute Localized Œdematous Type.

I shall not discuss the acute localized œdematous type.

Chronic Discoid Type.

The chronic discoid type is the commonest type. You are all familiar with the lesions on the skin. They consist of well-defined, erythematous, slightly infiltrated patches showing adherent keratotic scaling and follicular plugging.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on April 30, 1953. Dr. Perkins showed a number of lantern slides, many of which were lent by Dr. J. C. Belisario.

Older lesions show atrophic scarring. The lesions usually occur on the nose, the paranasal regions and the flush areas of cheeks, giving a butterfly or batswing distribution to the rash. However, they may occur on other parts of the face, and on the ears, scalp, neck, backs of the fingers and elsewhere. The vermilion border of the lip or the oral mucosa is sometimes involved, the lesions consisting of well-defined bluish-red patches with dilated blood vessels or narrow white lines. There are rarely any constitutional symptoms.

Chronic Disseminated Type.

In the chronic disseminated type multiple discoid lesions are more or less widely scattered over the skin and on the mucous membranes. On the hands and feet there may be scaly bluish patches. Constitutional symptoms are not striking, but not uncommon are mild symptoms and signs such as arthralgia, anæmia, leucopenia and albuminuria. The death rate is low.

A man, now aged forty-seven years, developed chronic disseminated *lupus erythematosus* whilst in the Australian army in the Middle East in 1940. Discoid lesions are scattered over the face, the ears, the neck, the "V" of the chest, the fronts of the forearms, the backs of the fingers and the hands and the backs of the heels. Over the following years he was given eighteen different treatments including injections of bismuth and gold without much benefit. Lesions on the forearms were excised by plastic surgeons in the Middle East, but the disease recurred along the edges of the grafts. Last year he was given mepacrine by mouth, 0·1 gramme twice or thrice daily, and during six months' treatment showed a little improvement.

The mepacrine treatment of *lupus erythematosus* was reported by Page (1951). It has been stated that this treatment was first used by Popoff in Bulgaria in 1941.

Subacute Disseminated Type.

In the subacute disseminated type the cutaneous lesions are erythematous scaling patches of varying size, which tend to be less well defined than in the chronic types. In about 17% of cases this form develops in a patient with chronic discoid lesions (Montgomery and McCreight, 1949). Large areas of the body may be involved, but the rash tends to be limited to the exposed surfaces including the "V" of the neck. Involvement of the lips and mucous membranes is common. The constitutional signs and symptoms vary in degree from mild to moderately severe. Distinction between this type and the following group is not sharp and depends on the degree of cutaneous and systemic involvement and the course of the disease.

Two male patients in their seventh decade, suffering from subacute disseminated *lupus erythematosus*, were treated by the method of Benson Cannon (1945), with *Liquor Iodi Aquosus* B.P. (Lugol's solution), three minims thrice daily being given by mouth at first and later five minims thrice daily. In both cases there was steady improvement. In one of the patients some lesions on the face took on the appearance of chronic discoid lesions, and these did not disappear until courses of intramuscular injections of "Rubyl" and "Myocrisin" had been given.

Acute Disseminated Systemic and Septic Types.

In about 6% of cases the acute disseminated systemic and septic forms develop in patients with chronic discoid lesions (Montgomery and McCreight, 1949). Sometimes this appears to result from treatment of chronic discoid *lupus erythematosus* with sulphonamides. However, they usually develop without antecedent chronic lesions. Sometimes the condition appears to follow prolonged exposure to strong sunlight. There are many cases in which prodromal and often severe constitutional symptoms precede by weeks or months the development of the rash. It is thought that in some cases the skin shows no visible involvement at any time.

The characteristic rash is a poorly defined or mottled erythema of the nose and cheeks, particularly of the butterfly area, the eyelids, the ears, and the "V" of the chest, accompanied by œdema of the face and eyelids. Involvement of the tips of the fingers is common. The rash may be widespread on the trunk and limbs and may resemble *erythema multiforme*. It may be purplish. Other forms of rash which may appear in addition or alone are purpura, cutaneous hæmorrhages, scaling patches, bullæ and vesicles. The lips often show pronounced œdema and crusting. On the oral mucosa there may be superficial ulcers with a yellowish slough.

The patients are gravely ill, and signs and symptoms of involvement of organs other than the skin are important and striking. They will be discussed by Dr. Helen Taylor.

In 1949 a girl, aged fourteen years, developed an erythematous rash on the butterfly area of the face, which was thought at first to be due to sunburn. However, ulceration appeared on the lower lip and the mucosa of the mouth and she became gravely ill. The eyelids became very œdematous, the ears and upper part of the front of the chest became erythematous, and bright red macules one centimetre in diameter developed on the backs of the fingers and the hands. She was admitted to hospital, where a number of investigations were carried out. A blood count showed that the red blood cells numbered 2,720,000 per cubic millimetre, and the white cells 7300 per cubic millimetre. The blood sedimentation rate was 14 millimetres per hour (Hawkesly's tube). Occasional red blood cells, and profuse hyaline and granular casts appeared in the urine. Urinary creatine excretion was 26 milligrammes per twenty-four hours, and the creatinine excretion was 74 milligrammes per twenty-four hours. The serum protein content was five grammes per 100 mils and the serum globulin content was 2·7 grammes per 100 mils. The blood serum failed to react to the Wassermann and Kline tests. The patient's temperature was 99° F. on her admission to hospital, and it gradually increased to 104·8° F. on the day before she died. Her death took place two months after the onset of the rash.

The rash of acute systemic *lupus erythematosus* may be confused with acute sunburn; but the latter clears up in a few days and does not involve the oral mucosa. In dermatomyositis the rash on the face is more heliotrope in colour, œdema about the eyelids is more prominent, muscle weakness and atrophy occur earlier and are more prominent, and creatinuria is present. Muscle biopsy reveals more pronounced nodular myositis and muscle degeneration, whereas leucopenia, anæmia, "false positive" results to serological tests for syphilis, and the L.E. cell phenomenon are usually absent. In pellagra the rash mainly affects the areas exposed to sunlight, particularly the face (where it may have a butterfly distribution), the backs of the hands and wrists and the "V" of the neck. The tongue is red and denuded and may be swollen and ulcerated, and there may be evidence of involvement of the gastro-intestinal tract and the nervous system.

Protracted Systemic Type.

In the protracted systemic type the skin manifestations are not striking, but there is a prolonged indefinite general decline with fever, arthralgia and loss of weight.

Discussion.

The question now arises whether these types are different forms of the same disease, differing in the severity and distribution of the lesions. Some authorities believe that the acutely ill patient with acute disseminated systemic *lupus erythematosus*, who is almost certain to die, must have a different disease from the patient with chronic discoid *lupus erythematosus* who has only a few blemishes on the face and feels perfectly well.

I cannot agree with this, for the following reasons:

1. The various types show a gradual trend in the clinical picture, from the first and second types with only skin lesions and no constitutional symptoms, to the fifth type, in which the patients are acutely ill with severe visceral lesions and sometimes no rash at all (Montgomery and McCreight, 1949).

2. The condition of patients is sometimes intermediate between these arbitrary types, so that it is difficult to decide to which category to assign them. It would be still more difficult to decide which patients should continue to be classified as suffering from *lupus erythematosus* and which patients should be assigned to the other disease causing the acute systemic manifestations.

3. Sometimes the acute systemic and disseminated type develops suddenly in patients already exhibiting a chronic form.

4. Histologically, the very recent lesion of chronic *lupus erythematosus* is identical with the cutaneous lesion of acute systemic *lupus erythematosus* (Michelson, 1952).

Conclusion.

In conclusion, I will recapitulate two points:

1. It is preferable to restrict "disseminated" to mean scattering of lesions over the skin, and to use "systemic" to convey the presence of constitutional symptoms and visceral signs.

2. There is a gradual trend between chronic discoid *lupus erythematosus* and acute disseminated systemic *lupus erythematosus*, so that as far as our present knowledge goes the various types appear to be different forms of the same disease.

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SYSTEMIC LUPUS ERYTHEMATOSUS.[1]

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SYSTEMIC *lupus erythematosus* has been described as now being as common as pernicious anæmia. It is certainly being found in increasing numbers of cases. The problem of diagnosis is seldom difficult when skin lesions are present, but when the systemic condition precedes or occurs without obvious skin lesions, the problem is usually a difficult one.

Dr. Vincent McGovern has kindly agreed to speak on the pathology of this disease; I will describe the clinical aspects.

History.

As long ago as 1872 Kaposi realized the systemic nature of the disease and its grave prognosis. In 1895 Osler emphasized the visceral manifestations, and in 1924 Libman and Sacks described the non-bacterial verrucous endocarditis. In 1935 Klemperer and others correlated the clinical and pathological features, and in 1936 Friedberg and others showed that it could occur without obvious skin lesions.

In 1948 Hargraves and others described the L.E. cell phenomenon. Recently, treatment with cortisone and corticotropin has stimulated further interest in this condition.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on April 30, 1953.

Clinical Features.

Females are affected more commonly than males. The incidence reported varies from 68% to 95%. Since diagnostic methods have improved, the sex difference is believed to be less.

The highest incidence occurs in women in the childbearing age, but this is found to be less marked than was formerly believed. The following analysis of 34 cases by Shearn and Pirofsky (1952) shows the range of ages: below ten years, three cases; eleven to twenty years, four cases; twenty-one to thirty years, eight cases; thirty-one to forty years, nine cases; forty-one to fifty years, five cases; fifty-one to sixty years, five cases.

Predisposing Factors.

Many factors have been implicated, but few can withstand critical analysis; young women who have red hair or inability to tan the skin are believed to be especially susceptible.

There is a high incidence of preceding exposure to sunlight, also of sensitivity to various drugs. Endocrine factors have been suspect, as the condition is often aggravated during the menstrual period; patients have been reported as having a remission throughout pregnancy, also as having an exacerbation during pregnancy with remission following therapeutic abortion.

Symptoms and Signs.

The basic lesion is one of fibrinoid degeneration of collagen with a predilection for the small arteries and arterioles. There may therefore be a wide variety of lesions, and the disease may present in many different ways.

Constitutional symptoms are extremely common. They consist of lassitude, fever, weakness and loss of weight. The fever may be of low grade, or there may be a high evening rise.

Polyserositis is an integral part of the disease. There is frequent occurrence of arthralgia, arthritis, and pleural, pericardial and peritoneal effusions.

The arthritis may attack one or more joints and may move from joint to joint, mimicking the changes found in acute rheumatic fever. Usually there is pain in the joints without objective change, but heat, swelling and redness may occur. Rarely deformities may occur similar to those seen in rheumatoid arthritis. The arthritis usually does not respond to treatment with salicylates.

Nausea, vomiting, and diarrhœa are common. Abdominal pain may be severe; it is believed to be due to perihepatitis, perisplenitis or abdominal adenopathy. Its main danger is that an operation may be performed if the underlying disease has not been recognized. The liver and spleen are commonly enlarged.

Much attention has been focused on the heart since Libman and Sacks described the verrucous endocarditis which has since been found in about one-third of patients at autopsy.

Systolic murmurs are commonly heard; they are usually soft and blowing, and in the presence of fever and anæmia it is difficult to assess their significance. Diastolic murmurs may also be heard—they can occur in early, mid or late diastole. They are usually associated with damage to the valves by verrucæ. However, it must be remembered that rheumatic valvular disease may also be present. Congestive failure occurs fairly often and is a common cause of death. Other findings are gallop rhythm, pericardial friction rub and pericardial effusion. Hypertension is often associated with renal disease.

The electrocardiographic changes have been well described by Liebow and Feil (1947). Flattening or inversion of the *T* wave is most common. Low voltage, prolonged *P-R* and *Q-T* intervals, auricular fibrillation and auricular flutter have all been described.

Retinal lesions are described by Maumenee (1940) as small, fluffy, yellowish-white to white spots and small hæmorrhages in the superficial layer of the retina and slight papillœdema.

Photophobia is common; conjunctivitis and subconjunctival hæmorrhages may occur.

Renal lesions are extremely important. They occur in almost all acute cases and in a large proportion of subacute cases. Hæmaturia (occasionally macroscopic) can nearly always be found if looked for microscopically; pus cells and casts are frequently present too. Proteinuria occurs in about two-thirds of the cases. The disease may manifest itself as nephritis, often resembling the nephrotic phase.

The pulmonary lesion may be chronic interstitial pneumonitis which leads to varying degrees of atelectasis with the usual signs thereof. Pleurisy and pleural effusion are common—cough, pain in the chest and hæmoptyses may occur.

Extensive focal and diffuse lesions of the central nervous system may occur (Glaser, 1952). The lesions are due to primary involvement of the smaller vessels of the arterial tree; this leads to focal or disseminated acute or chronic encephalomalacia, often with small cyst formations. The vascular lesions have a predilection for the grey matter of the cerebral cortex, particularly the perisulcal areas; the subcortical areas and the white matter of the cortex are affected less frequently and less severely. Neurological signs and symptoms may be absent in spite of widespread lesions in the central nervous system.

Signs and symptoms which do occur include focal and general seizures, transient cranial nerve palsies, hemiparesis and aphasia.

It must be remembered that generalized seizures may occur, especially terminally, in association with high fever or uræmia and in the absence of central nervous system involvement.

Acute toxic psychoses and delirium are also common terminally, and are not necessarily due to central nervous system lesions.

Peripheral neuritis has been described as a presenting symptom (Hepinstall and Sowry, 1952). It was considered to be due to ischæmic changes in the nerves produced by obliterative arteritis of the *arteria nervorum*. It is surprising that polyneuritis does not occur more often.

There is depression of all elements of the bone marrow. Anæmia is usually normochromic and normocytic. The patient may present with hæmolytic anæmia, and the response to Coombs's test may be positive.

Leucopenia is common; if severe, it is a poor prognostic sign. During intercurrent infections leucocytosis occurs.

Thrombocytopenia also occurs, and the patient may present with a picture suggesting thrombocytopenic purpura.

A high incidence of transfusion reactions (37%) has been reported.

Generalized enlargement of the lymph nodes is commonly found.

A false positive reaction to the Wassermann test is obtained in about half the cases.

Characteristic changes in the plasma proteins are a decrease in the serum albumin fraction and an increase in the serum α and γ globulin fraction.

The blood sedimentation rate is raised in all cases, usually considerably so, and usually remains raised even during clinical remissions.

The L.E. Cell Phenomenon.

In 1948 Hargraves and others (Hargraves, Richmond and Morton, 1948) reported the finding of two new cells in the bone marrow, the tart cell and the L.E. cell. Later it was realized that these cells could be found in the peripheral blood in the presence of an anticoagulant.

In 1952 Hargraves reported that these cells were found far more readily when peripheral blood was allowed to clot (Hargraves, 1952; Zimmer and Hargraves, 1952). The original bone marrow procedure was believed to have produced many false negative results; the new technique with blood clot preparation gives the danger of many false positive results unless a clear distinction is made between the tart cell and the L.E. cell.

The tart cell occurs especially in the blood of patients suffering from serious illness such as lymphoblastoma, pulmonary infections or metastatic carcinoma. It is also commonly found when the blood clot technique is used. The importance of the tart cell is that it may be mistaken for an L.E. cell. Hargraves describes the tart cell as follows (Hargraves, Richmond and Morton, 1948):

> This cell usually is a histiocyte or a "monocytoid reticulo-endothelial" cell that contains a second, characteristic nucleus usually placed in the Hof of the primary nucleus. This second nucleus nearly always stains reddish purple with Wright's stain in contrast to the dark purple nucleus of the histiocyte. This secondary nucleus shows a sharp nuclear membrane and the chromatin is definitely visible in a thick structural arrangement with relatively sharp differentiation between the chromatin and the parachromatin. Occasionally a cell is seen in which there are two such secondary nuclei, so that practically the entire cytoplasm is occupied by nuclear bodies. Except for this secondary nucleus the cell seems not to differ in appearance from the other histiocytes observed in bone marrow preparations. One can see this same phenomenon occurring in a mature neutrophilic polymorphonuclear leukocyte and less commonly in an eosinophil.
>
> The L.E. cell is practically always a mature neutrophilic polymorphonuclear leukocyte in contradistinction to the "tart" cell, which is most often a histiocyte. It seems obvious that the chromatin material is within a large phagocytic vacuole and all gradations of digestion of this material have been observed. While most of these cells characteristically show a homogeneous, purple-staining mass in the vacuole there are instances in which the chromatin pattern is still visible. For this reason it is essential that this cell be differentiated from the "tart" cell described in an earlier paragraph. Ordinarily this can be accomplished by finding numerous "L.E." cells in which the process of digestion has altered the appearance of this chromatin material, ranging from small smoky remnants of "digested" material to relatively intact nuclei indistinguishable from the secondary nucleus of the "tart" cell.

The L.E. cell phenomenon is an in-vitro phenomenon, and Hargraves considers that it is specific for *lupus erythematosus* provided that the interpretation of the cell is correctly made.

Differential Diagnosis.

The L.E. cell has become of great importance in recognizing borderline cases of systemic *lupus erythematosus*.

The usual form in which this condition is seen is in a young woman who complains of fatigue and arthralgia and is found to have mild fever, a tendency to leucopenia, elevation of the blood sedimentation rate and perhaps albuminuria. If a typical rash is not evident, careful questioning may provide a history of its occurrence. However, as has been shown, there are many variations from this picture.

Diagnoses commonly made before the correct one is made include the following. Acute or subacute rheumatic fever is the most common mistake, and it is a natural one in the presence of arthralgia, heart murmurs, fever, anæmia and raised sedimentation rate. Suspicion should be aroused by the failure to respond to treatment with salicylates and by the presence of leucopenia and of red blood cells in the urine.

Subacute bacterial endocarditis may also cause confusion, as besides the findings for rheumatic fever there will be an enlarged spleen and red blood cells will be found in the urine. Persistent failure to grow pathogenic organisms on blood culture and the absence of leucocytosis should raise doubts of the correct diagnosis.

Thrombocytopenic purpura or hæmolytic anæmia may be the form in which the condition first appears. It is necessary always in these cases to remember the possibility that systemic *lupus erythematosus* is the basic disease.

Pyrexia of unknown origin, chronic glomerulonephritis and sarcoidosis are diagnoses also likely to be made.

Treatment.

In assessing the effect of treatment it must be remembered that systemic *lupus erythematosus* is a relapsing disease subject to spontaneous remissions. The duration of the disease averages six years, with a range from seven weeks to twenty years.

General measures are rest, protection from sunlight, and nourishing food.

Mepacrine.

Page (1951) reports the accidental discovery of the value of mepacrine. The reduction in the skin lesions was judged much greater than when cortisone or corticotropin was used. There is also relief of the systemic lesions in the majority of cases.

The dose advised is 100 to 300 milligrammes given orally per day. Give a six to twelve weeks' course, then a small maintenance dose; or else give a four weeks' course followed by four weeks' interval. The mode of action is uncertain. It reduces the light sensitivity of the skin and also reduces photophobia; the more the skin is stained, the more effective it is. Side effects occur rarely, but are serious; they include dermatitis, lichenoid or exfoliative, aplastic anæmia, agranulocytosis, corneal œdema and opacities.

Cortisone and Corticotropin (ACTH).

Although most patients show rapid clinical improvement when treated with cortisone and corticotropin, relapses occur when treatment is suspended and also less often when a maintenance dose is given. The individual response to treatment varies greatly.

A large variety of treatment schedules has been tried. Suppression of fever is considered a useful guiding factor in estimating the dosage.

Dubois and others (1952) hold that treatment is most effective when a "Cushingoid" appearance is obtained; the remission can then be maintained with smaller doses. They advise starting with 40 to 60 milligrammes of corticotropin per day, given by the continuous intravenous drip method in a 2·5% or 5% solution of glucose in water. Gordon (1950) holds that continuous intravenous treatment is ten to twenty times as effective as treatment by intermittent intramuscular injections.

If the dose of 40 to 60 milligrammes per day fails to produce improvement it should be increased—as much as 600 milligrammes per day has been given.

In treating patients with these hormones, the usual precautions must be observed, and especially the tendency to infections and the danger of congestive heart failure must be kept in mind.

Adjuvant Measures.

Adjuvant measures also recommended by Dubois include the following: (i) a diet of low salt content, unless a salt-losing nephropathy is present; (ii) potassium chloride or citrate, eight to 12 grammes per day given orally, to counteract the hypokalæmic effect of the hormones; (iii) ascorbic acid, 500 milligrammes per day given orally, as more is said to be used during this therapy; (iv) testosterone propionate up to 500 milligrammes per day given intramuscularly. Such large dosage will not cause virilization during an exacerbation of the disease; when a remission occurs the dose must be reduced or virilization occurs. Only 10% of administered testosterone is excreted as 17-ketosteroids during an exacerbation, compared with a normal excretion of 40%.

It is likely that there will be considerable advances in our understanding of this disease in the near future.

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THE DETECTION OF THE RHESUS ANTIGEN AND ANTIBODIES: A SIMPLE AND RAPID METHOD.

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THE demonstration of the A B O antigens and antibodies rarely presents technical difficulties, but the Rhesus factor is hardly in the same category. In the first place, the supply of suitable Rh-typing sera is limited, and in the second place the Rh-agglutination technique requires more experience than is the case with the A B O groups.

It is the purpose of this paper to describe a technique which it is hoped will meet these difficulties.

Analysis of the Rhesus factor has shown that it is more complicated than was thought when it was first described by Landsteiner and Wiener in 1940. It is now known that there are six common Rh antigens in the human red cells —C, c, D, d, E, e, according to the nomenclature of Fisher and Race. However, it is the antigen D and its corresponding antibody anti-D which is responsible for some 95% of the dangers due to the Rhesus factor (Mollison, Mourant and Race, 1952). In hospital practice, the patient is tested for the presence or absence of the D antigen in the red cells, and when we say that a person is Rh-negative, it commonly means D-negative; similarly, Rh-positive means D-positive. While the other antigens and antibodies may occasionally cause intravascular hæmolysis, they must be investigated by special laboratories which have the necessary antigens and antibodies to carry out the tests, as it would be quite impracticable to supply all hospitals with these materials. The technique described in this paper is directed towards demonstrating the D antigen and D antibody, although the method is applicable to the other Rh blood groups.

A supply of anti-D serum is necessary for issue to hospitals for Rh testing. This serum must be obtained from D-negative subjects who have been immunized during pregnancy by a D-positive fœtus. Unfortunately, this serum does not often contain the "complete" anti-D antibody which agglutinates D red cells suspended in saline, as in the A B O blood groups. Usually the serum contains the "incomplete" antibody which will not agglutinate D red cells suspended in saline. The common practice is to carry out Rh testing with the complete anti-D antibody, but the supply of suitable serum is limited and is thus a constant source of embarrassment. The supply problem would be greatly eased if serum containing the incomplete anti-D antibody could be used.

Diamond and Denton (1945) showed that the incomplete anti-D antibody would agglutinate D red cells if the test was carried out in a protein-rich medium, such as 20% bovine albumin. Various methods have been devised for performing the test in albumin, but none of them have proved quite so practical and reliable for a hospital laboratory as could be wished.

In 1951 McNeil and Trentelman advocated the use of 10% polyvinylpyrrolidone (hereafter referred to as P.V.P.) in place of albumin, and showed that the test could be accelerated by centrifugation. Indeed, their results indicated that there was only a small loss of sensitivity if the preliminary incubation was eliminated and the reagents were spun immediately after they had been mixed. This work of McNeil and Trentelman is the basis of the technique described in this paper. In their original communication, McNeil and Trentelman were concerned with the titration of the Rh antibody, but subsequently, and while the present work was in progress, McNeil, Trentelman, Sullivan and Argall (1952) described a test for the routine detection of the Rh antigen. The test described by these American authors is essentially the same as the one described in this paper.

There are one or two minor disadvantages in using P.V.P., but if they are realized they can be guarded against, and the reactions are rather sharper with P.V.P. than with albumin.

TECHNIQUE.

The technique of the test is as follows.

Rh Typing of Cells.

Materials.

Red cells can be obtained from blood clot, finger-prick blood, or citrated or oxalated blood. The red cells need not be washed. Any incomplete anti-D serum with a titre of one in 64 or better can be used. It is absorbed to remove anti-A and anti-B antibodies. It should be kept frozen. The 25% solution of P.V.P. supplied by the manufacturers[1] is broken down by adding 1·5 parts of normal saline solution to 1·0 part of 25% P.V.P. "Merthiolate" is added to a concentration of one in 10,000, and after thorough mixing the pH is adjusted to 7·0 This 10% P.V.P. solution is kept in the refrigerator in a glass-stoppered container.

Notes on Materials.—It has been found that the D antigen deteriorates rather rapidly if the red cells are kept in dilute suspension, as in the "pilot" bottle which is ordinarily issued with the bottle of blood. However, if the pilot bottle contains blood in the same concentration as in the main bottle, the D antigen deteriorates more slowly and can still be detected after ten days' storage.

Anti-D serum with a titre of one in 64 or better will give easily-read reactions. Weaker serum can be used, but the clumps will be smaller and may be overlooked.

Method.

The method used is as follows.

One drop of 10% P.V.P. solution and one drop of the anti-D serum are placed in an agglutination tube (length 75 millimetres, internal diameter six millimetres is a convenient size). A platinum or nichrome loop (diameter of loop 1·0 millimetre) is dipped into the blood under test, and the blood in the loop is then mixed with the P.V.P. and serum in the agglutination tube.

The tube is rotated between the palms of the hands to mix the contents, and then centrifugated for one minute at about 2000 revolutions per minute.

After the centrifugation the tube is rotated between the palms of the hands until the button of red cells at the bottom of the tube completely disappears.

The tube is then inspected for evidence of agglutination. The clumps of cells in a positive reaction can be seen with the unaided eye, but a hand lens will help until experience has been gained. If the cells are D-negative, there will be no evidence of agglutination; but it is always advisable to confirm the reading by tipping the content of the tube onto a glass slide and examining it under the low power of the microscope—the cells should be evenly dispersed.

Notes on Method.—The amount of blood that is mixed with the P.V.P. and the antiserum is not crucial, but the reaction is somewhat easier to read if the resultant suspension of cells is pink, not red, in colour.

The practice of tapping the tube with the finger to resuspend the button of cells after centrifugation is not sufficient always to disperse D-negative cells and sooner or later will lead to error. There need be no fear that the clumps of D-positive cells will be dispersed by rolling the tube between the palms of the hands.

P.V.P. encourages rouleaux formation, and if D-negative cells are left in the tube for some minutes before being examined under the microscope, the rouleaux may be confusing. However, rouleaux can always be dispersed by rolling the tube again between the palms of the hands and examining the contents immediately.

Nothing is gained by incubating the tubes; indeed, if P.V.P. is left in contact with red cells at 37° C., the cells become much less sensitive to agglutination.

The incomplete antibody combines readily with the antigen on the red cells, whether the cells are suspended in saline, albumin or P.V.P. All that the albumin or P.V.P. does is to facilitate the clumping of the cells. The centrifugation packs the cells together and thus also encourages agglutination.

Bovine albumin can be used in this technique instead of P.V.P., but P.V.P. is cheaper and gives rather sharper reactions.

Findings.

Provided that the test blood is immediately available, the whole test can be carried out in five minutes with a minimum of equipment. The results are clear-cut and have proved reliable in thousands of tests.

The majority of red cells containing the comparatively rare D^u antigen are agglutinated in this test, although in some cases the agglutination can be detected only under the microscope.

THE PRESENCE OF RH ANTIBODIES.

A similar technique can be used for the detection of Rh antibodies in the serum of Rh-negative persons, the patient's serum and group O cells containing known Rh antigens being employed. However, the antibodies in the patient's serum may be weak and it is desirable to incubate the test material. A difficulty arises here—it was found quite early in this work that incubating red cells in the presence of P.V.P. weakens rather than strengthens the reaction. Therefore, in carrying out a test in P.V.P. for the detection of weak antibodies in a serum, it is necessary to carry out the test in two stages. In the first stage the known red cells are emulsified in the serum under test, and the tube is incubated (say for thirty minutes at 37° C.). In the second stage the P.V.P. is added to the tube and the contents are mixed. The tube is then spun and rolled between the hands to disperse the button of red cells, and the contents of the tube are examined for the presence of agglutinated cells.

It has been found that this test is not quite so sensitive as the indirect Coombs test in the detection of weak Rh antibodies.

CROSS-MATCHING.

The ordinary cross-matching test in saline detects A B O incompatibility between the donor's red cells and the

[1] That used in this work was kindly supplied by May and Baker, Limited.

recipient's serum. If the test is carried out in P.V.P. instead of saline, it will detect both A B O and Rh incompatibility even if the Rh antibody in the recipient's serum is incomplete.

Method.

One drop of the recipient's serum is placed in a tube, and one loopful of the blood to be transfused (usually from the "pilot" bottle) is emulsified in the serum. The tube is left at room temperature for fifteen minutes, and then one drop of 10% P.V.P. is added. The contents of the tube are mixed by rolling the tube, which is then spun at 2000 revolutions per minute for one minute.

The tube is rotated between the palms of the hands until the button of red cells completely disappears, and the contents of the tube are tipped onto a glass slide and examined immediately under the low power of the microscope for the presence of agglutinated cells (that is, incompatibility).

In an emergency the test can be accelerated by omission of the fifteen minutes of contact of the serum with the red cells. This entails a slight loss of sensitivity, but the longer contact is of importance only on the infrequent occasions when the antibody in the recipient's serum is very weak.

Notes on Method.—Workers who are used to the conventional macroscopic test to detect A B O incompatibility soon become accustomed to the microscopic test to detect both A B O and Rh incompatibility, which is described here. If the cells and serum are compatible, the cells will be seen to be evenly dispersed; if they are incompatible, clumps of agglutinated cells will be observed.

P.V.P. encourages rouleaux formation, but rouleaux will not be observed if the contents of the tube are examined immediately after centrifugation and rolling of the tube. Shaking or tapping the tube after centrifugation is not a reliable method of breaking up rouleaux.

Discussion.

It is a moot question how much of the investigation of the Rhesus factor should be carried out in hospital laboratories and how much should be left to the special laboratories attached to the Blood Transfusion Service. The question can be answered only by considering each of the several problems in turn.

Typing of Cells.

It would be quite impracticable to expect the special laboratories to carry out routine typing for the presence or absence of the D Rh antigen. If a supply of incomplete anti-D serum can be arranged for, there is no reason why the test described in this paper—or a similar simple test—should not be carried out in any hospital laboratory, wherever it is. Moreover, it is important that it should be carried out as widely as possible, because now that the danger of transfusing D-negative subjects with D-positive blood is appreciated, the call on D-negative blood will outrun the supply if this blood is given because of the possibility that the recipient may be D-negative.

However, if for any reason it is necessary to know the Rh genotype, that is certainly an investigation which can be carried out only in the special laboratory.

Testing for Rh Antibodies.

The problem of testing for Rh antibodies is probably better left to the special laboratory, as a number of Rh antibodies may be involved, and the special laboratory has the cells that are necessary for this investigation.

Cross-matching.

Incompatibilities remain the major hazard in transfusion therapy. The principal causes are carelessness (such as picking up the wrong bottle of blood), clerical errors, technical errors and Rh incompatibility. Carelessness can be guarded against only by better organization, clerical errors by cross-matching, technical errors by training, Rh incompatibility by a cross-matching test which will detect it.

The commonly used cross-matching test detects only A B O incompatibility, but all the authorities agree that it should be extended to Rh incompatibility. The authors of the authoritative memorandum Number 27 issued by the Medical Research Council of the United Kingdom (Mollison *et alii*, 1952) make the following statement:

> It is therefore essential in every transfusion to test the donor's cells against the serum of the recipient. Since albumin-agglutinating antibodies (especially anti-D) are a fairly common cause of potential incompatibility, and since such antibodies are the most likely to have been missed in previous tests, it is essential that a cross-matching test should detect them.

No doubt the main reason why the possibility of Rh incompatibility is not checked is the absence of a simple rapid test. It is hoped that the technique described in this paper, or a modification in the light of greater experience, will supply the need. It will detect in one test both A B O and Rh incompatibility, whether the Rh antibody is complete or incomplete, and it is practicable under almost any conditions.

The role of the special laboratory in cross-matching is to elucidate what has happened and is happening in an incompatible transfusion, and to give advice on the cause of a reaction in an apparently compatible transfusion.

The answer to the question that was posed at the beginning of the discussion is clearly that the special laboratory is essentially a reference laboratory. If it is expected to carry out routine Rh typing and compatibility tests, its major functions of supply and reference will suffer.

Summary.

A simple and rapid test for the detection of Rh antigens and antibodies is described. Use is made of polyvinylpyrrolidone (P.V.P.) to facilitate agglutination. The test is based on the work of McNeil and Trentelman, who advocated the use of P.V.P. for this purpose in 1951, and who, with their colleagues (McNeil *et alii*, 1952) subsequently reported favourably on a test very similar to the one described in this paper.

A simple cross-matching test which will detect both A B O and Rh incompatibility is proposed.

Acknowledgements.

I am indebted to my colleagues in the Blood Transfusion Service for a great deal of generous cooperation and help, and to May and Baker, Limited, for a supply of polyvinylpyrrolidone.

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NEUROSIS IN GENERAL PRACTICE.

By H. Owen Chapman,
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As this approach to the problem of neurosis in general practice is an unusual and very individualistic one, some explanation is required as to how and why it was undertaken.

After ten years' hospital and private practice in various parts of Australia, I was engaged for twenty-five years in

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hospital practice in Central China, and during the latter part of that period I had become increasingly interested in neurosis and its treatment. On returning to Australia in 1946 I was concerned to notice that, as it seemed to me, this disease was practically ignored and untreated by private practitioners, both in discharged soldiers and in civilians. As I decided not to start again in independent practice, I began to do intermittent *locum tenens* work, and once again it was the neurosis occurring in it that attracted me. I determined to make a special study of it, partly for its scientific and human interest, and partly to investigate its occurrence and treatment in private practice.

Scope of Investigation.

This investigation extended over the three years 1947 to 1949 and included 23 *locum tenens* assignments. These were in 13 different practices, the remaining 10 being reengagements. Some practices were large and wealthy and some quite small. One was situated in the inner suburbs of Sydney, one in the outer suburbs, one in Newcastle, one in a small far west grazing township and one on the Blue Mountains, two were in mining and industrial towns, one was in an industrial and one in an agricultural township on the coastal plain, and four were in grazing, agricultural and industrial towns and cities on the central tablelands. It is clear, therefore, that the scope of the inquiry includes a fair sample of the practices of the State, and that conclusions that may be drawn from it may reasonably be considered applicable to the whole system of general practice. The duration of the 23 appointments varied from seven to thirty-one days, with only one longer period of forty-nine days.

Delimitation of the Term "Neurosis".

The first question for investigation was that of the percentage of cases of neurosis out of all the patients examined in private practice. On this point I found the most wild and vague opinions commonly expressed by practitioners, such statements as "half my patients are neurotics" being sometimes heard. It was obviously essential to decide very carefully and precisely just what was to be the connotation of the word "neurosis". Without any attempt at a scientific definition, it may be stated that for the purposes of this investigation it is used to mean a disease other than a psychosis whose symptoms and signs are essentially due to emotional rather than to physical causes. For the sake of simplicity no distinction is attempted between hysterical conversion symptoms and neuroses, and mental symptoms are included together with physical signs.

It is necessary to avoid confusion in those numerous cases to which both emotional and physical causes contribute, and of course it must be recognized that there is an emotional or nervous factor inherent in every bodily reaction. When in such a disease as gastric ulcer or asthma the symptoms are always found to follow some form of emotional stress and always clear up when the stress becomes inoperative or is removed, such a case is included as a neurosis irrespective of whether the asthma is relieved by adrenaline or vaccines or the ulcer is relieved by alkalis or produces hæmatemesis or death. But when there is no more than moderate relief of the symptoms after the emotional factors have ceased of themselves or been effectively dealt with, the case is considered to be one of emotional reinforcement of organic disease and is excluded from this series. The few doubtful cases found have been so labelled and are not included.

Percentage of Cases of Neurosis Found.

In 22 of the *locum tenens* assignments there was a gross total of 3096 patients examined (with 1113 return visits), these figures including both surgery attendances and home visits, but not patients examined in public hospitals, military camps, mental hospitals and gaols. Out of these, 205 cases of neurosis were diagnosed, comprising 6·62% of the total number of patients. In the remaining assignment eight cases of neurosis were diagnosed, but these could not be included in the foregoing calculation, as the gross total of patients had not been recorded. By these 213 patients with neurosis only 61 return visits were made. There were also 11 doubtful cases of neurosis. In addition, six cases of psychosis were encountered during this work.

In the various assignments the percentage of cases of neurosis diagnosed varied from 2·4 to 13·8. But most of the extremes of high and low percentages were found in assignments of short periods of only one or two weeks, in which the smaller total of patients examined makes the recorded percentage of but little statistical significance. A study of the figures suggests that few, if any, of these practices, if carefully observed for a period of one or two months, would show a percentage of neurosis of less than five or over 10.

Difficulties of Diagnosis in General Practice.

There is another important consideration. It is by no means easy to recognize all the cases of neurosis presenting in the consulting room of a general practice. It is true that many patients show such a variety of symptoms, or symptoms of such a bizarre character, as could not be caused by any known organic disease; these are obvious and can be quickly diagnosed. But in many other cases it is only by continual alertness and by careful history-taking that the nature of the disease can be established, and unless a practitioner always keeps the possibility of such a diagnosis in mind, these cases will be missed.

It is also true that with increasing experience it will be found that more and more cases are recognized. In this series 6·67% of neuroses were diagnosed in the first 914 cases, 4·86% in the next 1090 cases and 8·33% in the last 1092; moreover, the percentage of 4·86 in the second group would have been appreciably higher had it not been that nearly half these patients (489) were examined in a very busy contract practice, in which the time available per patient was so short that only 3·5% of neuroses were recognized and undoubtedly a number were missed. From the foregoing facts we may infer that the 8·33% of the third group is much nearer the percentage in general practice than the average of 6·62% for the complete series.

Of the total of 213 patients with neurosis, 85 were males and 128 were females, but whereas in the first 103 cases the ratio of females to males was 49:51, in the last 110 cases it was 71:29. There were 10 boys and 15 girls aged eighteen years and under. Twenty-five of the adult males (one-third of the total number) were returned soldiers. The great increase in the preponderance of neuroses in females diagnosed in the latter half of the number of patients examined was doubtless due to increasing experience, which gave greater confidence in handling female patients and made it easier and quicker to establish *rapport* with them.

The following case is typical of those which will be missed unless the practitioner is careful and alert.

R.6., a sensible, capable-looking, quiet married woman, aged twenty-seven years, was examined three times for a very ordinary-looking *urticaria papulosa*, fairly widely distributed. In the course of treatment the following history was recalled. She had been very frequently troubled with it during the last seven years. She had consulted many specialists and been treated for allergy without improvement. After her marriage two years earlier the attacks had gradually dwindled to nil within a month. She was strongly sexed, and normal marital intercourse was happy and harmonious and had continued right through until she weaned her first child three months prior to examination. At that time she and her husband began to practise *coitus interruptus*, and almost at once the urticaria reappeared and had continued ever since. When a Dutch cap pessary was prescribed, she felt confident of cure, her intuition recognizing the cause of the disease. There was no time to work out the cause of its origin seven years before.

Comparison with Percentage in English Practices.

It is very interesting to compare the results of this investigation of the incidence of neurosis in general practice in New South Wales with those obtained in an investigation in England reported four years ago (Pemberton, 1949). This was a survey "undertaken to obtain information about the types and relative frequencies of illness which lead people to consult their general prac-

titioner". Eight general practitioners, six in Sheffield and two in neighbouring towns, for one week in summer and one in winter each kept a careful record of the diagnosis at every surgery consultation and home visit. The figures were then collated and analysed into 19 disease groups, that of "mental ill health" coming fifth in the list with a percentage of 6·5 of the total number of consultations. This group was further subdivided into neurosis 6·08%, psychosis 0·40%, and mental deficiency 0·02%, compared with neurosis 6·62%, psychosis 0·19%, and mental deficiency 0·00% in the New South Wales figures.

But, just as in the New South Wales figures, so in these English crude disease rates certain corrections need to be made. The time available for each patient in these English practices is in startling contrast with that in New South Wales. The total number of first and succeeding visits in 22 of the assignments of my investigation was 4209 in 62 weeks, averaging 68 attendances per week, and in the busiest contract practice, which is referred to above, the figure rose to 122 per week. At this latter rate of work it was found impossible, as has been stated, even to diagnose some suspected cases of neurosis, and undoubtedly a number were missed. But in the English practices reported on 4656 attendances were dealt with in fifteen weeks,[1] an average of 310 per week.

With work under these conditions, it is not surprising that the "miscellaneous and unclassified diseases" amounted to 7·3% of the total number, coming fourth in the list of 19 groups; and, if it had been possible to devote more time and care to the patients, we may be sure that many from this group and some from others such as "respiratory disease" (asthma), "digestive disease", "cardio(vascular) disease", "(obstetrics and) gynæcology", "skin diseases" and "neurological" would have been transferred to the category of neurosis. The indications therefore are that the actual incidence of cases of neurosis in English practices is probably higher than that, around 8%, which obtains in New South Wales.

Causes of Neurosis and the Difficulties of their Investigation.

In presenting a list of the causes found for the neuroses in my 213 cases, attention must be drawn to the special and heavy handicaps under which the general practitioner has to work. When a case of neurosis has been recognized, it is often quite impossible, with a full waiting-room in a busy practice, to give that unhurried and quiet consideration to the patient which is so essential to put him at his ease and win his confidence for inquiry into his symptoms. It is true that rarely a lot can be done even in half an hour or less, but often the patient must be asked to wait until the other patients are finished with, or to come for a special appointment out of surgery hours, as much of the work reported in this paper was done. But unless he realizes at this first interview that the doctor understands his disease, he is not likely to return, and in this way a number of patients are lost. Others suffering from obvious neurosis have always been used to treatment by placebos and want nothing else. There is also a special inhibition affecting a *locum tenens*: out of deference to drug or other treatment being carried out by the principal, courtesy sometimes forbids any investigation being undertaken by him.

Limitations of space have generally precluded the recording here of any more than the most essential or obvious cause in each case, though, of course, in many cases the neurosis is heavily over-determined by a number of causes. In many cases the only, or the principal, cause was disclosed in the course of the interviews, in others patients offered for consideration only the least important causes, while in yet others, such as some of the more severe anxiety states and the compulsion neuroses, the cause was obviously so deeply repressed that it would have been a mere waste of time to search for it in the short period of a *locum tenens* assignment.

[1] One week was missing, owing to a doctor's removal.

It will be seen that, in spite of these handicaps, it was in only 22% of the cases that no cause was found, and these included many in which it was deeply buried. In the other 78% of cases further investigation would probably have shown that the cause of a number recorded here was not the real one, or was only of secondary importance. But one of the welcome surprises of this study was that, in spite of all the handicaps and of the apparently superficial character of the work to which one was restricted, in the majority of this 78% of cases the cause was clearly recognized, not only by the doctor, but also by the patient, as was often evidenced by his or her emotional reactions. In some cases it lay quite superficially and was easily identified by the patient, but in others it lay more deeply and strongly repressed, and was recovered only at the cost of severe abreaction. The eight cases of juvenile asthma conformed to C. Swanton's full and illuminating description (1947) of the cause in the personality characteristics of the parents and of the necessity for their treatment, which, as he states, ought to be by the family physician.

Classification of Causes of Neurosis in 213 Cases.

The following tabulation sets out a classification of the causes of neurosis in 213 cases.

Frank Sexual Causes in Patients Themselves.

Sex traumata: infantile, with Œdipus complex, 1 case; childish, with guilt complex, 1 case; various, with guilt complex, 1 case; total, 3 cases.

Unphysiological coitus: *coitus interruptus*, 4 cases; use of rubber sheath, 1 case; uterine prolapse, 1 case; excessive coitus with fiancée, 1 case; sexual orgy with nymphomaniac, 1 case; total, 8 cases.

Frustrated love: hopeless liaison with married man, 1 case; incestuous love for brother, 1 case; lovers' quarrel or jilting, 3 cases; total, 5 cases.

Marital disharmony: wife patient, 2 cases.

Total cases with sexual causes in patients themselves, 18 (8%).

Sexual Causes in Others.

Parental disharmony in childhood, 4 cases; with sexual quarrels, 1 case; total, 5 cases.

Husband's adultery, 2 cases.

Husband's adultery and patient's vindictiveness, 2 cases.

Wife's adultery, 2 cases.

Father's adultery (daughter patient), 1 case.

Husband's impregnation of daughter, 1 case.

Wooed again, then rejected, by former husband, 1 case.

Total cases with sexual causes in others, 14 (7%).

Causes Associated with Pregnancy.

Prenuptial conception, 2 cases.

Wife's fear of pregnancy: first, 1 case; second, 1 case; third, 2 cases; fifth, 1 case; seventh, 2 cases; total, 7 cases.

Husband's fear of wife's pregnancy, 1 case; of abortion, 1 case; total, 2 cases.

Married woman's longing for pregnancy, 1 case.

Total cases with causes associated with pregnancy, 12 (6%).

The Fixations and "In-laws".

Mother fixation of husband (husband patient), 1 case.

Mother fixation of wife (wife patient), 1 case.

Mother fixation of husband and living with "in-laws": husband patient, 2 cases; wife patient, 4 cases; total, 6 cases.

Mother fixation of wife and living with "in-laws" (mother patient), 1 case.

Father fixation of daughter, 1 case.

Mother fixation of daughter, 1 case.

Living with "in-laws": wife patient, 2 cases; mother patient, 2 cases; uncle patient, 1 case; total, 5 cases.

Total cases with causes associated with fixations and "in-laws", 16 (8%).

Other Stresses Arising from Relatives.

Husband's inebriety, 1 case.

Husband's death, 2 cases

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Children's misbehaviour, 1 case.

Parents being neglected, 1 case.

Overcrowding of family quarters, 1 case.

Relative's disease: mother bed-ridden (heart disease), 1 case; mother has had "stroke", 1 case; mother-substitute old and feeble, 1 case; child has pulmonary tuberculosis, 1 case; child incurable cripple, 1 case; wife bed-ridden (heart disease), 1 case; wife has nightly asthma, 1 case; husband has nightly rheumatism, 1 case; total, 8 cases.

Total cases with causes associated with other stresses arising from relatives, 14 (7%).

Fear of Disease or Death.

Cancer: throat or larynx, 3 cases; uterus, 1 case;[1] vulva, 1 case; rectum, 1 case; intestines, 1 case; total, 8 cases.

Heart disease: heart disease, 5 cases; heart disease and coitus, 1 case; total, 6 cases.

Various diseases: inguinal hernia, 1 case; abscess on kidney, 1 case; snakebite, 1 case;[1] brain tumour, 1 case; pulmonary embolism, 1 case; chronic invalidity, 1 case; goitre, 1 case;[1] apoplexy, 1 case;[1] total, 8 cases.

Total cases associated with fear of disease or death, 22 (10%).

Occupational Stresses.

Frustration in relation to status or living conditions, 13 cases.

Unattainable standards of housework, 2 cases.

Fear of bankrupty, 1 case.

Retirement in idleness, 2 cases.

Stress of work and responsibility: business worries, 9 cases.

Total cases associated with occupational stresses, 27 (12%).

Battle Shock and Related Stresses.

Battle shock, 9 cases; prison camp, 1 case; war service, 1 case; total, 11 cases (5%).

Symbolic Causes.

Asthma: from diesel oil, incense, 1 case; from neighbour's (but not her own) backyard fire, 1 case; total, 2 cases.

Hay fever: from smoky motor-car exhaust, turpentine, kerosene, 1 case.

Total cases with symbolic causes, 3 (1%).

Miscellaneous Causes.

Remorse for causing friend's death, 1 case.

Senility's resentment of supplantation by youth, 1 case.

Oppression by thick uniform, 1 case.

Changeful anxieties and worries, 2 cases.

Heredity: hypochondriac mother and asthmatic daughter, 1 case.

Pleasure in invalidity and operations, 2 cases.

Total cases with miscellaneous causes, 8 (4%).

Juvenile Stresses.

Burdensome school responsibility (aged eleven years), 1 case.

Failure at school (aged fifteen years), 1 case.

Jealousy of sister's scholarship (aged seventeen years), 1 case.

Rejection complex since birth of brother (aged five years), 1 case.

Homesickness at first boarding school (aged fourteen years), 1 case.

Fear of school teacher: 1 patient aged eight years; (and of mother), 1 patient, aged eight years, 1, aged nine years; (and of school-mate), 1 patient, aged twelve years; 1, aged fourteen years; total, 5 cases.

Dominating, over-solicitous parents or mother:

(Asthma) 2 patients aged four and a half years, 1 aged nine years, 2 aged ten years, 1 aged eleven years, 1 aged eighteen years; (and various emotional stresses) 1 aged nine years. (Six of these patients were each the only child.)

(Hay fever) 1 patient aged twenty years; (and asthma) 1 patient aged five years.

(Mother patient) Son aged nineteen years, intending marriage, 1 case.

Total cases caused by parental attitude, 11.

[1] Only these four patients had any organic basis for their fear.

Total number of cases associated with juvenile stresses, 21 (10%).

Causes Not Ascertained.

Patient failed to return for second interview, 7 cases.

Insufficient time available, 24 cases.

Anxiety state, 9 cases.

Unsuitable for investigation, 5 cases.

Conditions unfavourable for investigation, 2 cases.

Total cases with causes not ascertained, 47 (22%).

Reports of Cases.

The following case illustrates how quickly the cause of a neurosis can sometimes be ascertained and dealt with.

On the day when I arrived to take over a certain practice my principal was taking me round to see a few patients before he left. We were called to see a woman (O.1.), about fifty years old, who for three days had been lying on a bed crying and refusing to talk. He immediately devoted all his attention to examining her and was absorbed in an endeavour to persuade her to get up and talk.

I put in the time talking to her married daughter, whose home we were in. She had been married three months earlier, and from that date her mother, who lived with them, every few days had had attacks like the present one. Before the marriage mother and daughter lived alone together. The daughter regretfully accepted the suggestion that her mother's condition was a jealous reaction to her own marriage. When I insisted that the mother must no longer live with them, she said that there was nowhere else for her to live—although it turned out that another daughter in the country would like to have her and the mother would like to live there. After her ejaculation, "But I don't want her to live with my sister!", she intuitively realized her own jealousy and saw that she must be cured of it if her mother was to recover and her own home was to be saved from wreckage.

By this time, about fifteen or twenty minutes after our arrival, my principal had made a diagnosis of hysteria and ordered treatment by sedatives. It was not until we were driving away that I had an opportunity to tell him of our conversation.

The following is a case in which the determining infantile traumata, which usually would require a lengthy analysis, were evidently only lightly repressed, and emerged into full recognition in the course of one interview of an hour—the only one that could be arranged.

W.9., a lean, introspective, unhappy-looking, tense returned soldier, aged thirty-two years, gave the following history and symptoms. He had had an inhibition against mixing in crowds. He had had a mother fixation all his life, and had never had a girl-friend until just the last month. There were many absentee gaps in his work. He had always had a strong aversion to receiving his wages which caused him a peculiar nameless feeling of guilt, this sometimes being so strong as to make him want to lose his job. He was obsessed with a peculiar discomfort of his lips and mouth which made him rub his lips, especially when men talked of sexual affairs.

From this statement he gradually but steadily worked back to the following experiences. At the age of eight years, one night in bed and subsequently twice in the orchard, he and his two brothers had practised mutual fellatio. At the age of seven years, one day he and his sister, two years older, had experimented with cunnilingus and fellatio. He had sucked vigorously and found it distasteful, and ever afterwards had succeeded in pretending to himself that he had not really sucked. He felt that his sister would despise him. At the age of three years he had tasted the fæces of another boy with whom he was playing mud pies, had found them nasty, and was ashamed of tasting another's fæces. Even now he gets an unaccountable bad taste when his obsession is working. When he was aged about two years his mother used to flourish her breast at him and try to get him to suck it, although he was averse to doing so and rather disgusted. Before he was three years old he had developed an Œdipus complex.

In this case the experience of guilt attached to receiving wages probably stirred up guilt feelings associated with an accentuated Freudian oral phase (the prototype of all later receiving) of early development. It is most unfortunate that, as the patient was capable of such insight, it was not possible to follow him up with assistance along the rocky path on which he had just set out, to reorientate and normalize his sex life.

The following case is illustrative of many where the patient's own reactions, breaking through resistance, identified the cause of neurosis beyond any possibility of doubt.

U.2., a woman, aged forty-five years, had had many years' treatment for her "nerves", including the administration of œstrogen and phenobarbital and "having everything taken away", all dating from a nervous breakdown nine years earlier. She had a desperate dread of meeting people, for which she could "imagine no reason". For many months she had had typical attacks of migraine. She had divorced her husband for a liaison with another woman, and thought it might be this which made her fear people's contemptuous remarks. She had, however, put him entirely out of her life. I remarked: "It is unusual and strange that, after nine years, you should still feel so keenly sensitive about your divorce. There are many divorcees about. Why do you think that people will specially despise you?" Presently her reserve disappeared and she told the following story.

In Scotland, at the age of eighteen years, she was deeply in love with a young man to whom her parents objected, so she married him secretly just before she emigrated with her family to Australia. There had been no sexual intercourse. He refused to follow her. Years later, believing such a marriage to be invalid, she contracted a happy and satisfactory marriage with an Australian. Her Scottish husband, hearing of this, divorced her. Her Australian husband then, hearing of him, contracted the liaison for which she divorced him. Her migraine began only when, after many years, the Scotsman started again a correspondence with her, reviving all her old love and desire for him, then rejected her and returned her letters unopened. When she was asked whether it was not this rejection which caused her dread of meeting people, with tears and much distress she admitted that it was, and that her attacks of migraine were connected with the course of her relations with him. Then, after some hesitation, she admitted that the present and most severe attack followed her repression, after a struggle, of a longing to go to Scotland after him.

The interview which is outlined above occupied one hour in the patient's flat.

The following is one of those cases in which, out of deference to the principal, no investigation into causes could be considered.

C.5., a married woman. aged thirty-nine years, had been subject to hay fever, often severe, and indigestion for twenty years. The taking of hydrochloric acid for the last three years had practically cured the latter. There was strong evidence from her history that allergy to grass pollens had been at least one potent cause of the former. For three years she had been receiving vaccine treatment by a well-known specialist against the proteins of wheat, plantains, rye grass and coryza, of which she had now become immune to the first two. She had had three years' treatment with rye grass vaccine, and in this fourth year was having doses of the strongest titre. Her attacks in the first three years had greatly lessened; but in the fourth year they had relapsed very badly, to the consternation of herself and her doctor. She also said that attacks were brought on by (*a*) the smell of kerosene, (*b*) even the smell of turpentine in bath cleaners and floor polishes, and (*c*) especially the smell of petrol from a smoky motor-car exhaust or from city buses. And she added that the attacks had continued throughout a long sea voyage (during which she would hardly find rye grass).

Experience of similar cases strongly suggests that the foregoing three causes were merely symbols of historical emotional stress, and that this was a case with both emotional and physical contact determinants. It was tempting to invite the patient to talk about emotional stresses at the age of nineteen years, when her attacks had first begun, but I forbore and gave her yet another injection of rye grass vaccine.

Symptoms and Signs of Neurosis and their Significance.

The symptoms and signs of neurosis, whether psychosomatic or purely psychic, have not the same definitive and obvious diagnostic value as have many of those in organic disease. Indeed, precisely the same type of emotional stress may produce entirely different sets of symptoms in different patients. This is well illustrated in the lists of symptoms in the following four cases: (i) K.3., recurring herpes on the right upper lip for two years; (ii) M.3., nervous dyspepsia, no interest in life, failure of libido, fear of pregnancy, fear of losing younger husband's love, inability to continue her work, ability to talk only in a whisper, absolute despair (attempted suicide); (iii) O.17., severe precordial discomfort and vague pains across upper abdominal zone on setting out for home after holiday; (iv) Q.11., severe migraine for two years, perpetual fatigue (neurotic type), uncontrollable bad temper with her children, frequent weeping, feeling of desperation (left home with her children). There was exactly the same cause for each of these very diverse symptom complexes—namely, living with a mother-in-law for whom the husband had a strong fixation. But the only obvious cause which was indicated by each of these syndromes was emotional stress, evidently severe in M.3. and Q.11.; however, the precise nature of this stress, in these as in all cases of neurosis, was a very personal and individual matter for joint inquiry by the doctor and patient. And for such inquiry the symptoms at best may serve as symbols and sign-posts in a cryptic language which needs careful and skilful interpretation.

The symptoms, then, in the following classification are not presented with the suggestion that they are diagnostic of anything else than emotional stress. It is true that with experience the practitioner soon learns to recognize that certain symptoms are commonly associated with particular kinds of stress and so may be a useful and quick guide to the cause, but the nexus is seldom certain in any particular case until the patient himself confirms it.

This classified list is included rather as an illustration of the wide and varied scope of the symptoms of neurosis that are week by week passing through the consulting rooms of the general practitioners of New South Wales. Much more elaborate and comprehensive lists of symptoms, including many that are unusual and bizarre, may be found in the literature. But those lists have usually been compiled by psychiatrists who have culled them from an experience of many years in this specialty. The symptoms in the present list, on the contrary, all presented, and a number of them dozens of times, in sixty-two weeks in average general practices in the State. This is not to say that general practitioners necessarily hear anything like this variety of symptoms from their patients who suffer from neurosis, but such are the symptoms for which patients seek, and urgently need, relief, and of which they are ready and often only too eager to tell a doctor who "understands their case".

Classification of the Symptoms and Signs in 213 Cases.

The following tabulation sets out the symptoms and signs in 213 cases:

Symptoms and Signs of Collapse.—Weakness, fainting, giddiness, sweating, tremors, shivering, "wobbly" abdomen.

Sensory Disorders.—Paræsthesias (generally transient) of lips, of glove and stocking pattern, of various other areas. Pains (usually not corresponding with anatomy, physical signs or bodily activities) of back and spine, of throat (with dysphagia) or of various other parts of body, or general aching. Cramp in limbs. Transient deafness or amaurosis. Headache, tinnitus, noises, vertigo, "bursting feeling" or nameless discomfort in head.

Motor Disturbances.—Loss of power in limbs (especially legs). Spasmodic movements of hands, fidgeting and jerking. Twitching of face (especially), of lumbar region, of iliac region, of limbs. Tremor of voice, stammering, and transient whispering, unintelligibility or aphonia.

Dermatoses.—Macular eruption, labial herpes, pustular dermatitis (scattered), facial erythema, "nerve rashes", *urticaria papulosa* (scattered), *urticaria papulosa* (stocking and glove pattern), hypertrophic dermatitis of palms, cheiropompholyx.

Cardio-vascular Disorders.—Precordial discomfort, palpitation, tachycardia, pseudo-angina, hyperpiesia.

Disorders of Generative System.—(i) Male, pain on ejaculation, impotence, fear of coitus; (ii) female, amenorrhœa, dysmenorrhœa, oligomenorrhœa, menorrhagia, menstrual irregularity, dyspareunia, vaginismus, perineal and anal pain (at coitus), fear of coitus, repression of libido.

Abdominal Disorders.—Anorexia, abnormal hunger, flatulence, nausea, retching, vomiting, irregular diarrhœa or constipation, or both, loss of weight. Epigastric pulsation, "twitching and churning". Abdominal discomfort, pain and tenderness—zonal (especially lower abdominal zone), scattered and indefinite (generally not corresponding with anatomy or any morbid entity), colicky, like labour pains.

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Phobias and Compulsions.—Agoraphobia, claustrophobia, fear of suffocation, fugues, unreasoning flights from home, abnormal sleepiness, guilty dread of receiving money, cyclic polyuria, dread of meeting people, nameless fear, compulsion to murder.

Multiple Fears.—Fear of a disease (especially heart disease), of insanity, of impotence, of permanent incapacity, of death, of relative's death, of bankruptcy, of family's future, of desertion by younger husband.

Anxiety and its Accompaniments.—Strained facies, worry over everything, exasperation over details, discontent with every arrangement, failure of concentration, failure of memory, feeling of inadequacy for responsibilities, inability to work, "has had everything taken away" (by abdominal surgeon).

Depression and its Accompaniment.—Depression, worry, distress, tiredness of neurotic type, ennui, loss of interest in occupation, loss of initiative, insomnia, repeated weeping, irritability, feelings of guilt, resentment or hostility, hopeless misery, refusal to talk, impulses to suicide, suicide.

Special Syndromes.—Migraine, asthma, hay fever, gastric ulcer, duodenal ulcer, chronic colitis, pseudocyesis, hysterical seizures, psychasthenia, hypochondriasis.

Stresses Insecurely Repressed.—Restlessness, irritability, starting at noises, tension, "black-outs", unreasoning violent tempers (especially towards own children), impulse to scream, muttering, heavy drinking, terrifying dreams, seizures of battle neurosis.

Classification of Methods of Treatment Used in 213 Cases.

The methods of treatment used are set out in the following tabulation showing grouping of patients and classification of methods.

A. Environmental Treatment.

Readjustment of environment or circumstances: removal to another district or appointment, 4 cases; eviction of "in-laws", 3 cases; change of school, 2 cases; hospitalization until change of residence, 2 cases; readjustment of routine and conditions within home, 3 cases; legal separation, 1 case; increase of pension, 1 case; holiday, 8 cases; total, 24 cases.

B. Physical Treatment.

(i) Operation: repair of hernia, 1 case; thyroidectomy, 1 case; removal of cyst over larynx, 1 case; uterine suspension, 2 cases; total, 5 cases. (ii) Prescription of Dutch cap pessary, 8 cases. (iii) Reassurance by demonstration, 9 cases. Total cases in which physical treatment was given, 22 cases.

C. Psychic Treatment.

(i) Interview with other people: mother or parents of child, 9 cases; daughter, 1 case; husband—refused to come (listed under Group E), 3 cases; husband—came, and wife's cure assured, 1 case; total, 11 cases. (ii) Good prognosis (for environmental treatment already initiated by patient), 3 cases. (iii) Rational treatment, 62 cases. (iv) Rational treatment with effective transference, 1 case. (v) Rational treatment, facing basic moral problem, 2 cases, (vi) Rational treatment, facing basic religious problem, 2 cases; total, 81 cases.

D. Referred Elsewhere for Treatment.

(i) Institutions of Repatriation Department, 6 cases; (ii) special hospital clinics, 4 cases; (iii) specialists, for clinical examination and reassurance, 2 cases; (iv) psychiatrists or psychoanalysts in private practice, 6 cases; total, 18 cases.

E. Neurosis Not Treated.

(i) Symptomatic drug treatment or placebos given, 7 cases; (ii) treatment deferred to later appointment, which was not kept (*a*) by patient, 8 cases, (*b*) by husband, 3 cases—11 cases; (iii) not suitable for treatment, 14 cases; (iv) no opportunity for treatment—in most cases for lack of time, 36 cases; total, 68 cases.

Discussion.

A consideration of this tabulation will suggest how varied and comprehensive are the methods required for the treatment of the neuroses met with in everyday practice. There is no other disease requiring such a wide therapeutic range—as wide potentially as the activities in the lives of the patients. But there is one unifying principle, the "rational" method, which gives effective guidance and perspective for all other methods used.

From the point at which a doctor arrives at the tentative diagnosis of neurosis, the treatment increasingly becomes an intimate, friendly, reasoned, cooperative inquiry by doctor and patient into the disease of the latter, leading to their progressive understanding of it and recognition of its causes. As progress is made the patient, with the doctor's aid, achieves clearer and clearer insight; he finds his disabilities suddenly or gradually losing their strength; of his own initiative or at the doctor's suggestion he begins to take positive action, mental, physical or social, in the direction of untrammelled, healthy and normal life. Recovery implies such readjustments as these, and they are the measure of its progress. This is the reason why treatment should, whenever possible, be carried out in the patient's usual social environment rather than in an institution or a distant town. It will thus be seen that, although the use of the rational method has been listed as the outstanding procedure in only 62 of the cases, it is also the method with which treatment in every case begins, and which leads to and indicates every other form of special treatment or adjustment required.

It is, of course, in this field of treatment that the drastic curtailment imposed by the term of practice of *locum tenens* is most crippling. If there had been an opportunity to carry the treatment of these patients through to a conclusion, various other special methods would have come into use. As it was, only the most urgent and obvious adjustments could be recognized as necessary and arranged for, as listed in sections A and B of the tabulation. The operations were advised to deal with structures which had become the basis of crippling symptoms. The use of the Dutch cap pessary was prescribed in cases in which fear of pregnancy had become an obsession and made coitus a nightmare, or in which *coitus interruptus* was making an emotional wreck of the wife and at times of the husband. There is no other single method of treatment used which evoked such invariable gratitude in the patient and such confident assurance of cure.

There is a common belief that the best routine treatment in general practice is "reassurance", by which is meant hearty and emphatic statements that the disease (of which the doctor has not found the cause) is "doing well" and that the placebo prescribed by him will strengthen the patient and "build up his nerves". The only patients to whom such treatment is rightly applicable are the very small number (1% in the first tabulation) who are really happy with their illness. But it is quite useless for curing any patients, if for no other reason than that the patient has already had long evidence of its failure. The suggestion, if put over skilfully, may effect a temporary improvement; but, as the cause remains, the disease will reassert itself, as every practitioner knows. There is, however, another kind of reassurance by demonstration (third tabulation, section B (iii)), which deals specifically with an ascertained cause and has a definite place in therapy.

D.10., a woman, aged sixty years, complained of throat symptoms, present without signs, for three months. Investigation brought to light that she had nursed a sister until she died of cancer of the throat after much radium treatment. This had developed after a thyroidectomy. The patient herself had recently undergone a thyroidectomy, and now was so obsessed with the fear of cancer of the throat that she could only speak of it in a whisper. As the initial step in treatment she was sent to an ear, nose and throat surgeon for an exhaustive examination and reassurance.

A whole book would be necessary to discuss the subject of rational treatment; only a few practical observations are possible here. Although the general attitude towards these patients has been that of Rogers's non-directive therapy (Rogers, 1942), the extreme limitations on time have made it little more than an attitude. An interview begins with a friendly and encouraging invitation to the patient to tell more about the symptoms that he complains of or about any others that come to his mind. But he is also urged to follow up any clues that appear in this recital.

Dates are of inestimable value. It is surprising how often a patient will state that severe, perhaps nearly crippling, symptoms appeared, apparently without any

cause, at a particular date in his past history. A quiet and assured explanation that such symptoms, appearing as these did, could be due only to emotional stress of some kind, followed by a short description of the usual kinds (fear, anxiety, frustration *et cetera*), will often be countered by an emphatic denial of any such cause—too emphatic and a little uneasy. A gentle but confident insistence that there must have been some such experience at that time, and finally a friendly "Why not tell me about it? You'll feel better after you have" will often break through the resistance and bring the basic cause to light, sometimes with pronounced abreaction. The way is then open for leading the patient towards insight into his symptoms and a positive attitude in dealing with his problems.

Several times a patient has been able to bring a significant dream which was a valuable aid; and in one case (L.6.), with only three or four formal interviews, but under peculiarly favourable accompanying circumstances, a sound transference was actually established which was of great service in achieving a recovery. But such classical aids are, of course, not usually available under the conditions of work of a *locum tenens*.

Sections C (v) and C (vi) of this tabulation contain two cases each in which the whole syndrome of the disease was traced down to a basic moral or religious problem, recovery depending on its being effectively dealt with. In such cases the practitioner needs to be priest as well as physician. Experience of more leisured work on patients not included in this series leaves no doubt that, if it had been practicable to follow all these cases through, a good many more would have been reduced to such basic problems.

The Results.

In this series of cases it is the results that are the hardest feature to report on. Indeed, no precise and comprehensive report is at all possible. In the case of nearly all the patients in groups A, B, C(i) and C(ii) of the third tabulation, the treatment was arranged for, but not carried out, during my tenancy, so that the result could not be observed. Of the 18 cases in group D, it was only in three that an acknowledgement was received.

However, for the patients in groups C(iii), C(iv), C(v) and C(vi), the treatment, being psychic, was concluded with the last or only interview, and many of these by their observed emotional reactions and intellectual responses showed with considerable clarity the result of their treatment. To these have been added those of group B(ii), most of whom also showed plainly their reaction to the anticipated freedom from sexual distress. Of these 75 patients, many during a single interview showed such evidences as abreaction indicating a freeing of repression, insight (faint or clear) into the cause of their symptoms, a reorientated and positive attitude towards their problems, confidence that they were cured, a noticeable change in facial expression from the time of entering the consulting room, or spontaneous and eager gratitude for what had been done for them. A few others, with more than one interview, reported fading of symptoms and positive action in resuming normal life, while yet others showed such results during my second term of duty in the same practice or wrote reporting by letter. In the largest group the result of treatment was quite conjectural. These results may be summarized as in the following tabulation.

Classification of Results in Five Treatment Groups of the Third Tabulation.

The results in sections B(ii), C(iii), C(iv), C(v) and C(vi) may be tabulated as follows (75 cases):

(*a*) Some cooperation, insight and hope	13
(*b*) Fair to good insight, symptoms relieved, more confidence and more cheerful attitude	8
(*c*) Clear insight, reorientation of attitude, confidence of cure	9
(*d*) Satisfactory readjustment, freedom from symptoms, complete recovery	8
(*e*) Religious problem faced and solved, great relief	2
(*f*) Clear insight into moral problem, but no solution	2
(*g*) No evidence of result available	33

Of the 213 patients, 169 had only one interview, 27 had two interviews, 12 had three, 2 had four and 3 had five. An indication of the improved results that can be secured with even such slight increases in the total interviews as these is to be found in group (*d*) above. Of these eight patients, three had three interviews, three had two interviews and two had one interview.

Reports of Cases.

S4, aged sixteen years, an intelligent schoolboy, provides an example of the short and trivial cases. For three months he had been afraid of appendicitis because of severe lower abdominal pain whenever he played the bagpipes. (He had no tenderness except a trace over the left iliac fossa.) He also thought that he had strained his abdominal muscles lifting a sheep a few weeks earlier. (But he had often exerted himself more strenuously.) It was noticed that he wore extraordinarily light clothing for winter weather, but he said he could never stand thick clothes. He then told how he never played the bagpipes except in the band uniform, which was "terribly thick and uncomfortable" especially under the belt (lower abdominal zone). The patient was shown how his fear of appendicitis, strained muscle and bagpipes was a subconscious expedient to relieve him of the intolerable discomfort of his uniform, and he was told to return to his home and blow his bagpipes hard for an hour out of uniform.

D4 was a returned soldier with a long-standing war neurosis, cured after two interviews. He came to ask for a certificate for an invalid pension, because he always felt so excessively tired that he was unable to cope with his work. He also had a right facial tic, specially active whenever he talked of his war experiences, at which times he was apt to fall asleep. On his discharge eighteen months before he had done well as a station manager until he felt that the owner was putting an impossibly heavy burden on him, when the onset of this pathological tiredness made him resign. Then he bought a farm; but now, when the fight to make good seemed rather hopeless, again the tiredness crippled him. Recently he had numbness in both hands. At length he came to talk freely of his experiences on the Siam railway, where he was given impossibly heavy tasks while suffering from the severe diarrhœa and weakness of pellagra. He began to see the fortuitous association between an impossibly heavy and hopeless task and pathological tiredness. The facial tic was associated with the strongly repressed memory of a bitterly resented blow on that spot by a Japanese with a cane, the numbness of hands with severe ulceration of fingers almost needing amputation. On my return two years later he reported that the tic had disappeared at once and the paræsthesia of hands in one or two weeks, while the tiredness had entirely cleared up in a month, leaving him quite well.

M3, aged forty-two years, is the patient whose symptoms are described in the section on symptoms and signs. I examined her on a spring morning while she was lying on a bed in a little shack on the mountains at the end of her tether. Her husband had found her standing naked, drenched in sweat, fascinated before a bath full of water. After a while she told me all her trouble. They were returning to Sydney that night. She promised me to consult an obstetrician about having a baby, to consult immediately a psychiatrist whom I recommended, and not to commit suicide until after he had had a chance to talk with her. When I brought her his letter I found her much better, bright and cheery. Three days later she returned the letter by mail, saying that she now felt all right, so she would not need it. Thoroughly alarmed, I sent it back at once, saying that she was far from being cured and must be treated. As it went to the post there came a long-distance phone call from her, in a frightened voice, asking for the letter back because she had relapsed badly. I heard later that she had made a good recovery.

Comparison with Cases in Specialist Practice.

The picture of neurosis and its treatment shown by this series of cases reveals a great contrast with that in nearly all books based on specialist practice. In most of the cases met with in general practice the active cause is not buried so deeply, nor is the resistance so strong, and probably a smaller percentage of neuroses have a sexual origin.

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But the most startling difference lies in the duration of the treatment required. One, two or three years are the common periods recorded in psychoanalytical journals and text-books—absolutely impracticable alike for the general practitioner and the great mass of neurotics awaiting treatment. But the reports from general practice submitted here,[1] though obviously and admittedly very sketchy and incomplete, indubitably suggest a period approximating much more nearly to Carl Rogers's (1942) estimate of "six to fifteen [weekly] contacts rather than fifty" and his statement that "where maladjustment is not extreme, where the individual is not deeply neurotic, two, four or six contacts are often sufficient for the client to find the needed help".

The chief causes of this difference are that the patients treated by specialists have in the past been drawn almost exclusively from the relatively small group with severe chronic neuroses (Alexander and French, 1946) which are beyond the reach of the general practitioner. The aim of specialists also is to give the patient "a complete insight into the causes of all his behaviour" (Rogers, 1942), whereas the general practitioner merely aims to assist him to "move forward independently" and symptom-free to "healthy self-directed action". The essential practical point is that the great majority of neurosis cases presenting to the general practitioner are either acute neurotic breakdowns or mild chronic cases, both of which are usually practicable propositions within his competence.

The Problem of the General Practitioners.

It would be very unrealistic to discuss the problem of neurosis in general practice without considering the practitioner. The outstanding feature of the problem in New South Wales is that general practitioners appear to take no interest in its treatment. A close study of the *British Medical Journal* for the last six years shows, especially in the correspondence columns, occasional communications from general practitioners indicating that in England there is at least a minority who do seriously treat this disease in the routine of their practices (Clark, 1947; Eve, 1948); and C. A. H. Watts has written an article (1948) showing how effectually this can actually be done. In the United States today there is both in the medical profession and in the general public a veritable boom of interest in psychiatry (Buckle, 1953). But a scrutiny of the last six years' files of THE MEDICAL JOURNAL OF AUSTRALIA gives no evidence whatever of such activity by our general practitioners, though there has been an increasing number of articles by psychiatrists. Dr. D. F. Buckle (1953) writes:

> There is a fear of psychiatry, and a consequent resistance to its advance, in the mental attitudes of the community including its medical members. . . . This tremendous burden [the treatment of neurosis] is being carried by school teachers, social workers and the patients' families with negligible help from the medical profession, many of whom just do not know what to do when these patients arrive in their surgeries . . . but most conditions can be diagnosed only by medical examination.

Of the 21 doctors (including some in partnership) whose practices I saw from the inside, it was only in three that I saw any sign of interest in neurosis; two of these appeared to make an effort to treat it.

The causes of this aloofness are not far to seek. The medical curricula in Australia give practically no training in the theory or practice of this therapy, and very few practitioners have done any reading on it for themselves. The majority, indeed, are temperamentally quite unsuitable for it; most extraverts, for example, instinctively shrink from a consideration of personal emotional problems, being quite convinced that they have none themselves and often rather contemptuous of those who show that they have. The time factor is also a very real one, for though there are odd patients who can be cured in half an hour's conversation, the classical hour's quiet and uninterrupted interview is still the standard for most, where it is essential for the establishment of confidence and *rapport*. In addition to these obstacles, it is obvious that, from the short point of view, the practitioner must be prepared to accept some financial sacrifice, for the patient, though taking three to five times as long as one suffering from a physical disease, will generally expect to pay only the same fee.

But it is unthinkable that we should be content to be turned aside by these obstructions. Let us not allow the frequent absence of physical signs and the low death rate to blind us to the severity of this disease. Though there were some comparatively trivial cases in this series, there were many in which it caused serious or complete incapacity and disablement—far more serious than in the average of the cases in a practitioner's waiting room. If it had been practicable to record more case histories, it would be realized better how many patients there were who suffered from intense unhappiness and acute bodily pain and distress. Others were faced with the imminent loss of their livelihood, poverty or the break-up of their family. One was driven to an attempt on her life. It is only by a refusal to face the facts that this situation can be tolerated with complacency. Nor is the disease negligible quantitatively. Let us always keep before us the fact that it accounts for about 8% of our daily patients. Let us also remember that it hits particularly heavily our fellow Australians who fought for us overseas—33% of the adult males in the series being returned soldiers and 15% patients with battle neurosis. Nearly all of the latter group were severely ill, but eminently curable, and yet, eight years after the end of the war, they were derelict, with no effective treatment either in base hospital or in private practice.

Our medical profession is not to blame for the development of this problem, as it is only in recent years that we have understood something of its nature and treatment; but it will be a disgrace for us if, now that we do understand it, this huge mass of serious and crippling illness continues to go untreated. It is the greatest therapeutic problem confronting us today, whose final solution must remain for future years and a new generation of medical practitioners and statesmen. But a beginning can be made now. Practitioners, to be successful in this work, need no diplomas in psychiatry or experience in mental hospitals. (Resident work among the psychotics of the Mental Hospital, Orange, from 1950 to 1953 has given me a deeper understanding of the patients with severe neurosis and a more confident touch in handling them, but it was by no means essential to such work in general practice.) But doctors for this work should be "introverts who have achieved a workable degree of extraversion". They should be men sensitive to, and keenly interested in, the human aspect of their practice. They must be prepared to read a little—not necessarily much. Freud's "Interpretation of Dreams", Ross's "Common Neuroses" and Rogers's "Counselling and Psychotherapy" are fundamental. For guidance in the actual technique and practical problems of analytical work, it is hard to find any book suitable for the general practitioner. Lorand's "Technique of Psychoanalytic Therapy" (International University Press, New York, 1946) covers the ground and has a chapter of essential importance to the beginner on counter-transference. Alexander and French's "Psychoanalytic Therapy" (Ronald Press, New York, 1946) is a little more advanced; but it does deal well with many of the problems of practice and with the transference.

Though an exceedingly busy practice might absolutely contraindicate it, for a doctor who is somewhat less busy it should be practicable to arrange for two or three hours' interviews a week with a selected patient or two to feel his way along. Patients must be educated to pay higher fees for this exacting psychiatric work, as they already do for operations and also for X-ray examinations, which are much less demanding on the energy and time of the doctor; and this should not be difficult as his reputation for the work rises and spreads. (One patient even in this exploratory series, for whom a neurosis arising from sexual excess had been resolved in less than half an hour's interview, insisted on paying a double fee.) But, of course,

[1] See fourth tabulation and what follows.

the change in the rate of charges would take a little time to establish.

Though the monetary return may be low, the intangible reward, for those who can appreciate it, is high. With increasing experience in thus dealing with the life problems of men and women, the zest for the work grows. Moreover, there is no other branch of practice, except perhaps obstetrics, which wins such generous and heartfelt gratitude from the patient, who feels that his doctor has understood and helped him in an intimate way never experienced before.

This article is written for general practitioners on the basis of experience in general practice. It is submitted with full realization of the unsatisfactory nature of the report, arising from the extremely discontinuous and fragmentary character of the clinical material available. The much wider conspectus thus gained may, however, be some compensatory advantage in pioneering a new field. It is hoped that there may be others who can report on a steady, uninterrupted and therefore more successful series of cases in their own practice.

SUMMARY.

This article is a report on the neuroses found in 13 average general practices in New South Wales in the course of 23 *locum tenens* assignments for periods of from seven to forty-nine days each.

Out of a total of 3096 patients, a crude average of 6·62% of cases of neurosis was found. From this a corrected neurosis rate of 8% of the patients in New South Wales practices is calculated.

This compared with a crude neurosis rate of 6·08%, but a corrected rate of over 8%, found in a somewhat similar investigation in England.

The difficulties of diagnosing and treating neuroses in general practice are described and illustrated.

The very wide range of causes and the signs and symptoms found are classified, and the significance and interpretation of the signs and symptoms are discussed.

The methods of treatment used are classified as environmental, physical and psychic treatment and reference to specialists; rational (analytic) treatment, essential in all cases, is briefly described.

Those results which were available under the conditions of *locum tenens* work are reported on and show appreciable percentages of greater or less improvement and of recovery. The effect of the handicap produced by restriction of available time is shown.

Case histories are quoted to illustrate the various features described and the results reported.

The contrast between specialist and general practice in neurosis is stressed and its significance for general practitioners pointed out.

The problem presented to the body of general practitioners by this untreated mass of illness is discussed in its various aspects, and suggestions are made for tackling it.

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I wish to express my thanks to Dr. A. L. Kinna and Dr. Hugh Fraser for valuable criticism and advice.

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THE PREPARATION AND STABILITY OF FIELD'S STAIN.

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It has been known for many years that the nucleus of the malaria parasite in blood films when treated with simple stains consisting of mixtures of methylene blue and eosin will not stain a red colour. Only when the methylene blue fraction is altered by oxidation is the nucleus differentially stained. Such oxidized products are known as "polychrome methylene blue" or "azure". In German nomenclature Roman numerals are used in referring to these materials as azure I and azure II, azure II consisting of a deliberate mixture of equal parts of azure I and unchanged methylene blue. For these same materials American terminology refers to azure A and azure B. Roe, Lillie and Wilcox (1940) state that the proper synonym for azure I is azure B, and not azure A as has been supposed, and this confusion of synonyms probably accounts for the poor results hitherto obtained with Giemsa solutions manufactured in the United States.

Field (1941) described his stain, which required the use of two separate aqueous solutions A and B. Solution A consisted of an aqueous solution of methylene blue and commercial azure I, and solution B was a 0·2% solution of eosin. Both solutions were buffered to pH 6·6, and at the same time rendered isotonic to blood with phosphates. The aqueous medium represented a departure from previous methods of preparation, in which the oxidized methylene blue eosin complex was dissolved in methyl alcohol (as in the Leishman or Wright stain) or a mixture of equal parts of methyl alcohol and glycerin (as in the Giemsa stain).

The use of Field's stain depends on slight fixing without the use of methyl alcohol, followed by rapid staining before the parasites are washed from the slide. Staining occurs in a matter of seconds against the minutes required by former procedures.

Prior to 1939 most of the commercial azures were of variable quality. Exceptions such as Grübler's Giemsa stain were made by an undisclosed process, and produced good staining of the parasite—clear blue cytoplasm and red nuclear chromatin. Most British and American azures were made by heating the material with alkali (sodium bicarbonate), but even with elaborate methods of factory control the product consisted of variable mixtures of lower azures (further oxidation products); these materially impair the stability and staining properties, giving an ill-defined grey-lilac shade to plasmodial and lymphocyte cytoplasm, and a dense red-purple colour to the nuclear chromatin. With films so prepared differentiation of the nucleus from the cytoplasm is extremely difficult because of the similarity in these shades.

Also, for the preparation of the single methyl alcohol solution it was necessary to carry out precipitation with eosin, a complex which was dissolved in the alcohol. Field's two aqueous solutions avoid this precipitation, and the present investigation was concerned with a modified method for the preparation of Field's solution A, and with its stability especially in view of the variation in composition of the available azure powders.

Spectral Standards.

The spectral properties of a solution may be expressed by measuring the degree of absorption that occurs at different wave-lengths, and the variation in absorption that is shown by different mixtures of methylene blue and azure B was investigated by Lillie (1944*a*). His results are summarized in Table I.

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De Burgh (1946) has stated that wide variation in the percentage of azure B makes little difference to the staining quality, without indicating any limits. Lillie and Roe (1942), however, observed that the best stains show their maximum thiazin absorption usually between 650 and 660mμ; that is, by trial and error it was found that the best differential stains are obtained when the methylene blue component is so altered by oxidation that the point of maximum absorption drops from 667mμ to between 660 and 650mμ. Hence, from Table I, it may be assumed that at 653mμ the solution consists of approximately equal parts of methylene blue and azure B.

TABLE I.
Variation in Absorption of Mixtures of Azure B and Methylene Blue.

Azure B : Methylene Blue Ratio.	Wave-Length of Maximum Absorption (mμ).
10 : 0	645
9 : 1	645
8 : 2	646
7 : 3	647
6 : 4	651
5 : 5	653
4 : 6	655
3 : 7	657
2 : 8	659
1 : 9	663
0 : 10	664

During a study of the effect of acid methods, Lillie (1942) investigated such common oxidizing agents as potassium dichromate, potassium permanganate, mercuric oxide, silver oxide and sodium iodate, and found that the chromic acid oxidation gave azures of quite constant spectrophotometric properties, when the same ratio of potassium dichromate to methylene blue was used. Thus the oxidation could be controlled with such reproducible results that he described (Lillie, 1943) a method for the laboratory preparation of Giemsa stain. This dichromate oxidation was used in the present work of directly preparing Field's solution A, several different brands of methylene blue obtainable locally being used.

Choice of pH.

It was decided to buffer the stock solution to pH 6·6, since Lillie (1944*b*) had shown that the preparations obtained by redissolving the oxidized methylene blue-eosin complex in methyl alcohol were more stable in acid than in alkaline solution. Also, Field had observed that his stains had good tinctorial properties at this pH.

Experimental Investigation.

Field's solution A was prepared directly as follows.

Methylene blue, five grammes of 86% or an equivalent quantity of other labelled strength, was dissolved in distilled water, 300 millilitres, in a one litre Florence flask. Sulphuric acid, 3·4 millilitres, was added, and the solution brought to boiling point. Solution of potassium dichromate (10%), 10 millilitres, was added, and the boiling continued gently for twenty minutes. The neck of the flask was sealed with a suitable funnel, and small quantities of distilled water were added at intervals to keep the level constant. The solution was cooled under running water, and neutralized by the cautious addition of sodium bicarbonate (10 grammes required); 50 grammes of sodium phosphate ($Na_2HPO_4.12H_2O$) and 25 grammes of potassium phosphate (KH_2PO_4) were added, and finally the solution was diluted to 500 millilitres.

The solution was just acid (pH 6·6—glass electrode) as intended, and before it was used in staining, one part was diluted to four parts with distilled water. The staining properties of the solution when used in accordance with the directions given by Field were excellent. The absorption measurements, discussed later, were found to be in agreement with those obtained by Lillie, 200 milligrammes of dichromate being used per gramme of different brands of American methylene blue, calculated on the 86% basis.

Table II summarizes the preparation of the solution with different brands available locally. The amount of dichromate was kept constant and the amount of methylene blue increased to compensate for any deficiency from 86% strength. With unknown samples an amount was taken on the assumption that the strength was between 80% and 86%, since 80% is the minimum for medicinal quality. It was thought that the dye content of some samples might have been greater than this, but from the slightly lower absorption maximum it would appear that all samples of British origin were of 80% strength.

The original samples were read[1] at 2mμ intervals, and the final readings were taken at 5mμ intervals when it appeared that little alteration had occurred.

The solutions were stored at room temperature (20° to 30° C.) in the dark in corked full bottles without preservative, some as concentrate and some in diluted form.

After two-year and five-year intervals, the pH and the staining and absorption properties were again examined.

Results and Discussion.

The reaction was still within 0·1 of the original pH 6·6. The staining properties were still excellent and absorption measurements showed that within the accuracy obtained with the instruments used, no alteration had occurred.

At one stage it was thought that it might be necessary to keep the stain at a lower pH, and adjust it before use. However, the results show that this procedure is not necessary.

Summary.

In view of the uncertain staining properties of most commercial azures used for the identification of malaria parasites in blood films before 1940, a simple method for the direct preparation of Field's stain (solution A) from methylene blue has been investigated. Spectral examinations have led to the conclusion that the oxidation of different samples of medicinal methylene blue (at least 80% strength) may be controlled to give reproducible preparations with maximum absorption at approximately 650mμ. The staining solutions are then free from undesirable lower azures, are very stable, and possess excellent tinctorial properties.

[1] The earlier measurements were made with a Hilger-Nutting spectrophotometer. Later a Beckman model DU quartz spectrophotometer was used.

TABLE II.

Sample.	Origin.	Labelled Methylene Blue Content *per Centum*.	Amount of Methylene Blue Used for Preparation of Solution. (Grammes.)	Maximum Wavelength, Solution Just Prepared. (mμ.)	Maximum Wavelength After Storage for Two Years. (mμ.)	Maximum Wavelength After Storage for Five Years. (mμ.)
I	Australia.	—	5·3	648	646	648
II	Britain.	—	5·4	650	646	648
III	Britain.	—	5·2	647	648	648
IV	Germany.	—	5·2	650	648	647
V	U.S.A., NA 22.	82·0	5·2	651	650	647
VI	U.S.A., CA 23.	83·2	5·15	653	650	653

Acknowledgements.

The earlier absorption measurements were made in the laboratories of the New South Wales Government Analyst, and later work was done at the New South Wales University of Technology. One of us (A.K.S.) wishes to thank the chairman of the Repatriation Commission for permission to publish this paper.

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THE MORTALITY FROM TETANUS IN AUSTRALIA.

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TETANUS has not been a large cause of mortality over the years of my mortality survey, 1908 to 1945, in the civilian population of Australia at any rate; but since it is a preventible disease it deserves some mention.

In general, deaths certified as due to tetanus will be assigned by the official statisticians to the rubric "tetanus", according to the rules of assignment of the *International List of Causes of Death*. Those cases in which tetanus followed on some rather mild accident, such as an abrasion or penetrating wound, will be invariably assigned to the rubric "tetanus". However, after severe accidents, when tetanus is regarded as a terminal incident, the death will be assigned to one of the rubrics covering violence and accidental deaths, and puerperal tetanus will be assigned to some rubric in the class of puerperal deaths. Some doubts may arise that tetanus and tetany may have been confused in the mind of the statistician classifying the deaths. I have at different times raised this question with the official statisticians, and it appears that these two entities have not been confused. We may assume then that the official statistics give a fair indication of tetanus as a cause of death. The age distribution of the deaths may be studied in the accompanying table, which brings out the relatively high mortality in the first year of life, followed by lower mortality rates at ages one to four years. The rates are then higher for the ages five to fourteen years, the school years, when the child is exposed to minor abrasions and to penetrating wounds of the feet. The rates remain relatively constant throughout adult life. The male rates at all ages tend to be higher than the female owing to differences in activities at school and occupations in adult life. There has been a great decline in the rates over the years 1908 to 1945 in the first year of life and a moderate decline at ages five to fourteen years; the improvement at all other ages has been disappointing, if we except the war years, 1941 to 1945. Nor can we indicate any fall due to the increasing use of passive immunization after the first World War. It is difficult to know whether the marked fall in the male rates among those of the military ages may be due to withdrawal of men from civil life to the armed forces or whether active immunization may not have been important. I have therefore determined the rates for three post-war years, for which this effect has persisted. This fall, then, cannot be interpreted as being due to withdrawal of men from the population at risk, but must be ascribed to active immunization in the armed forces during the war and perhaps in a less degree to immunization in the forces since. It indicates that a worthwhile drop in the rates can be obtained by active immunization. The effect of active immunization in preventing tetanus in war has been discussed by Bensted (1940) and by Boyd and MacLennan (1942). It appears that active immunization is an effective prophylactic.

The deaths in 1911 to 1920 may be studied in more detail to get a better idea of age incidence. For the males, in the first five years of life, there were 165, nine, nine, 16 and 15 deaths; 107, 86 and 56 deaths occurred at ages five to nine, ten to fourteen and fifteen to nineteen years respectively. The corresponding numbers of female deaths were 104, eight, 12, nine, 10, 26, 22 and 10. A more detailed analysis of the deaths in the first year of life is not available. One may interpret the deaths in the first year of life as being largely due to *tetanus neonatorum*, although it cannot be denied that some deaths may have been merely due to "tetany". Then for a few years the incidence of deaths is low; but over the school ages the incidence for boys rises before falling again to adult life levels. The changes can no doubt be attributable in a large degree to the absence or presence of footwear.

The age distribution of the deaths from tetanus suggests that prophylactic injections of toxoid should be given as early as possible. It appears that now a number of women will have had injections of toxoid, and therefore the presence of antibodies in the child's blood may interfere with the production of tetanus antibodies. Sauer and Tucker (1950) have found that injections at the ages of three, four, five and six months give complete protection to the child. Di Sant'Agnese (1950) gave the injections at an earlier age and believed that protection was thereby

TABLE I.

The Mortality from Tetanus in Australia.

Period.	Sex.	Deaths per Annum per Million at Risk at Ages (Years).											
		0	1 to 4	0 to 4	5 to 14	15 to 24	25 to 34	35 to 44	45 to 54	55 to 64	65 to 74	75 and Over.	All Ages.
1908 to 1910	M.	324	19	88	46	30	9	22	26	33	25	—	35
1911 to 1920	M.	246	21	75	38	19	12	18	22	29	27	22	29
1921 to 1930	M.	84	23	36	32	16	11	13	12	16	23	22	20
1931 to 1940	M.	20	23	23	31	20	10	10	16	19	16	18	18
1941 to 1945	M.	21	25	24	32	7	2	4	9	12	15	18	13
1946 to 1948	M.	10	17	27	24	10	3	7	10	16	24	12	14
1908 to 1910	F.	262	12	66	10	6	7	8	9	4	6	—	15
1911 to 1920	F.	163	17	51	10	4	6	6	6	8	4	9	12
1921 to 1930	F.	48	8	16	12	3	3	6	6	8	4	7	7
1931 to 1940	F.	14	13	14	9	2	4	4	5	5	5	6	6
1941 to 1945	F.	8	8	8	8	2	4	3	5	2	9	6	5
1946 to 1948	F.	4	6	10	9	3	3	1	4	4	12	12	5

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given. Both these authors used the method of triple immunization, so that they combined the inoculation of tetanus toxoid with those of pertussis and diphtheria, and indeed this seems to be the most practicable public health measure for combating them.

Summary.

Tetanus has been a fairly constant but not large cause of mortality in Australia for many years. The statistics fail to show a fall indicating the introduction of passive immunization, but do indicate that active immunization is of value. The male sex has been more subject to tetanus than the female over the years 1908 to 1945.

Acknowledgements.

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Reports of Cases.

A REPORT ON TWO CASES OF MALROTATION OF THE GUT IN CHILDREN.

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Case I.

DIANA, aged five weeks, was admitted to the Townsville General Hospital on November 29, 1952. Her birth had been normal, and her birth weight was eight pounds nine ounces. She was breast fed. At the age of three or four days she began to vomit her feeds. Vomiting was intermittent at first, but at about two or three weeks she vomited after nearly every feed. The vomiting was projectile and occurred any time up to one hour after feeds. At three weeks her food was changed to "Vi-Lactogen". Vomiting ceased for one week, then recommenced. For three days prior to her admission to hospital she had vomited everything, including fluids. The vomitus had been bile-stained for the preceding thirty-six hours. She had had no bowel motion for two days.

On examination, she was seen to be a very emaciated infant with a scaphoid abdomen; her weight at five weeks was only nine pounds six ounces. Within a period of three hours, while rehydration was being attempted, she developed profuse vomiting and rapidly became profoundly dehydrated. Her heart rate was 160 per minute, her temperature was 102·2° F., her abdomen was tense and no masses were palpable.

A diagnosis was made of malrotated gut with duodenal obstruction.

A laparotomy was performed on November 29. The stomach and duodenum were dilated. A volvulus of the small bowel was present. There was malrotation of the gut, with a band across and compressing the duodenum. The volvulus was untwisted; the gut was viable. The first part of the colon, caecum and ileum were freed from the peritoneum, and the caecum was placed in the left hypochondrium.

After the operation, intravenous replacement therapy was carried out. On November 30, at 7.45 a.m., the patient vomited bile-stained fluid; gastric suction was begun. In the afternoon she passed three small offensive motions containing mucus and blood. Penicillin was administered. On December 1 the administration of oral fluids and gastric aspiration were commenced. On December 2 she was absorbing fluid orally. Intravenous therapy was stopped. On the same day she was started on weak "Vi-Lactogen" feeding. On December 4 she had no vomiting, but developed diarrhœa and became dehydrated. Her oral intake of fluids was increased. On December 6 200 cubic centimetres of serum were given. Oral feeding was continued. On December 8 expressed breast milk was given. She began vomiting bile-stained fluid. Intravenous therapy was instituted, combined with gastric suction. Her abdomen was distended. Bowel sounds were present. On December 9 intravenous therapy was stopped and she was given lactic acid milk orally; to this she responded well.

On December 10 the child was rehydrated and taking oral feeds well, and she had no vomiting. On December 11 and 12 she had occasional vomiting only. On December 18 she was described as "holding her own". On December 19 she developed pneumonitis followed by pneumonia. On December 21 she was given 200 cubic centimetres of group O Rh-negative blood. On December 22 antibiotics were given. On December 23, at 4.00 a.m., the patient died from lobar pneumonia.

The parents would not consent to a post-mortem examination.

Case II.

Heather, aged eight years, was admitted to hospital on May 14, 1951, with a past history of having undergone a Rammstedt operation for pyloric stenosis when she was an infant. Ever since, the child had been subject to recurrent attacks of abdominal pain and vomiting. For the past twenty-four hours she had had diffuse abdominal pain. The character of the pain was uncertain, as the child was somewhat backward mentally. She had vomited all fluids taken in the past twenty-four hours.

On examination of the patient, she had a furred tongue and her breath was "abdominal". A mass was palpable in the right iliac fossa, but there was no true rigidity. Her temperature was 99·4° F. Her pulse rate was 120 per minute.

A provisional diagnosis was made of acute appendicitis with omentum surrounding the appendix.

At operation, the whole jejunum was distended and full of fæcal masses of the consistency of sand. There was volvulus of the small intestine, and the caecum was lying free near the duodeno-jejunal flexure, the small and large intestine having a common mesentery. The stomach was dilated.

The volvulus was untwisted and the peritoneum overlying the duodenum was incised. This appeared to be the constricting band.

Another unusual abnormality was that only the jejunum appeared dilated, and this dilatation extended to where the jejunum went through a rent in the mesentery. This was extracted and the rent was oversewn. The caecum was placed in the left side of the abdomen.

After a fairly stormy convalescence of one week the child recovered completely, and no abnormality could be discovered on examination of the abdomen. X-ray examinations by means of barium meals on June 12 and October 16, 1951, revealed no constriction of the duodenum or small bowel, and barium was in the colon for four hours, with the caecum overlying the duodeno-jejunal flexure.

Commentary.

In Case I it may appear from the post-operative vomiting that the obstruction was not completely relieved. However, the passage of normal motions containing bile seems to point to the fact that the obstruction had been relieved. In our opinion, the stormy post-operative convalescence was mainly due to handling of the bowel in an infant who was in a state of gross shock before operation, with resultant ileus.

In Case II the pre-operative diagnosis was incorrect. The unusual feature was the double lesion: (i) malrotation of the gut with obstruction of the duodenum, and (ii) jejunal obstruction where the jejunum passed through a rent in the ileal mesentery. Whether this patient also had pyloric stenosis, or whether the vomiting in infancy was due to malrotation, is open to question. The pylorus appeared normal at operation. The history of a previous Rammstedt operation was not available.

Discussion.

Spencer (1951) describes in detail the different types of malrotation which may occur. Our two cases present different clinical and pathological findings.

The diagnosis in Case I was obvious; on the other hand, in regard to Case II, we still think that we might miss the pre-operative diagnosis in a case of a similar nature.

Summary.

A report of two cases of malrotation of the gut is presented. In Case I, there was fixation of the caecum in the right hypochondrium, with an obstructing band across the duodenum from the caecum. In Case II, the mesentery was common to the small and large bowel, with a volvulus, and the duodenal obstruction was reduced by the right leaf of the mesentery compressing the duodeno-jejunal flexure. Volvulus occurred in both cases and was probably the precipitating factor causing the duodenal obstruction.

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BILATERAL GIANT RENAL CALCULI.

By L. GANZ, M.B., F.R.C.S. (Edinburgh), M.R.C.P. (Dublin),
Gympie, Queensland.

IN a recent article in the *British Medical Journal*, giant calculi found *post mortem* have been described. In the following case the stones, although not so large, have been removed by bilateral nephrolithotomy and the patient is doing very well indeed.

Clinical Record.

Mrs. E.S., aged thirty-seven years, came to the out-patient department on July 29, 1952, with pain in the right iliac fossa, continuous in character, of approximately six years' duration. She also had scalding on micturition, but to her knowledge she had never passed any blood in the urine. Examination revealed nothing abnormal except some tenderness along the right ureter; the kidneys were not palpable. One point of interest in her past history was the fact that she had had hypertension over the last six years, her blood pressure being always in the region of 170 millimetres of mercury, systolic, and 110 millimetres, diastolic. The pain in the right side was interpreted as being due to chronic appendicitis; the appendix was duly removed three years ago, without any benefit to her. It was, therefore, assumed that she was suffering from chronic pyelitis and she was treated accordingly with sulphonamide drugs and was given *Mistura Potassii Citratis cum Hyosciamo* for years, again without any effect.

In view of this history it was decided to investigate her urinary tract. An excretion pyelogram revealed the presence of a large calculus completely filling the pelvis and the much dilated calyces of each kidney, and a poor concentration of the contrast medium. Examination of the bladder by the cystoscope gave negative results. Other urinary findings are shown in Table I.

The blood urea content was 76 milligrammes per 100 millilitres. The urine submitted for investigation was insufficient to determine the specific gravity.

I explored the right kidney first. It was exposed through a lumbar approach. The organ, which was enlarged, was found adherent to surrounding structures. After mobilizing the kidney I split it from pole to pole; the renal substance varied in thickness from one to six millimetres. As a matter of fact, when the upper renal pole was delivered the stone was exposed accidentally; the rim of tissue covering it was about the thickness of paper. The calculus was removed by being broken up into five pieces and each fragment was delivered separately from the distended calyces and pelvis. One loose spherical stone 12 millimetres in diameter was also extracted. Hæmostasis was attended to, a drainage tube was left in the renal pelvis and another drain in the perirenal space, and the wound was closed in layers.

The patient was in a state of severe shock at the end of the operation, but responded well to treatment. She was given two pints of blood, four pints of serum, one litre of 4·2% sodium sulphate solution and two litres of glucose saline solution. Streptomycin and penicillin were administered for three days. Her subsequent recovery was quite smooth; the drain was removed on the second day and the nephrostomy tube on the tenth day. She was ambulant two days later and discharged home fifteen days after the operation, the wound perfectly healed.

The blood urea level steadily rose after operation; the highest reading was 153 milligrammes *per centum* on the third day; it reached its original level of 76 milligrammes *per centum* on the tenth day. An excretion pyelogram taken two months after the operation showed that the right kidney was clear of stones and function was reasonable.

The patient was readmitted to hospital on October 20 for removal of the stone from the left side. The blood urea content on her admission to hospital was 41 milligrammes *per centum*. A urea concentration test showed that the right kidney was concentrating better than the left. I exposed the left kidney on October 31 through a lumbar incision. The same technique was employed to remove the calculus as previously. Control of hæmorrhage was rather more difficult. The rim of renal tissue around the stone varied from four to eight millimetres in width. In addition to the main large calculus I found three free smallish

TABLE I.

Source of Urine.	Excretion of Indigocarmine.	Red Blood Cells.	Pus Cells.	Albumin.	Urea.
Right kidney	8 minutes.	+++	+++	+++	1·5 grammes per 100 millilitres.
Left kidney	4 minutes.	–	Occasional.	+	1·0 gramme per 100 millilitres.

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stones, each about the size of a pea. The post-operative treatment was the same as previously, and she was discharged from hospital on the fifteenth day. This time the blood urea kept at a steady level of 42 milligrammes *per centum*.

At present both kidneys are clear of stones, and excretion and concentration of "Uroselectan" are satisfactory. The stones were reconstructed in the dental department to their original shape and form (Figure I). Both are phosphatic calculi, the right measuring 12·5 centimetres by 6·5 centimetres, the left 8·5 centimetres by 5·0 centimetres.

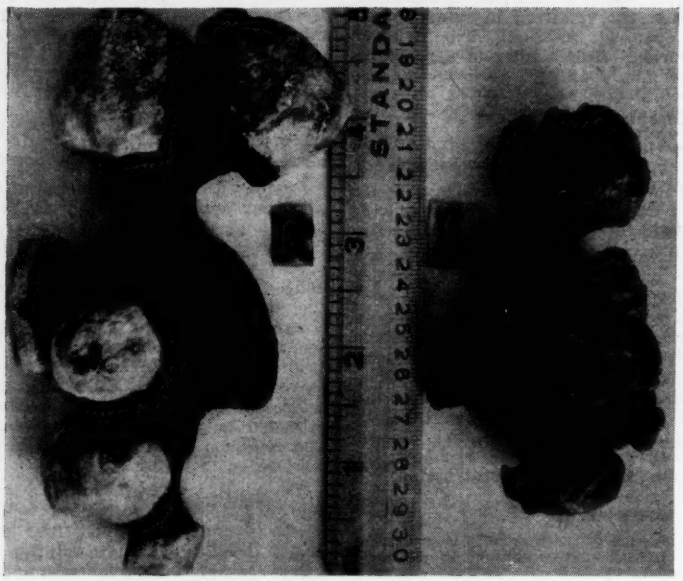

FIGURE I.

Acknowledgements.

My thanks are due to the medical and nursing staff of the General Hospital, Gympie, who meticulously carried out the post-operative treatment, and also to Mr. J. F. Watson, of the dental department, who reconstructed the stones with great skill and patience.

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CASE OF MESENTERIC VASCULAR OCCLUSION IN A PATIENT SUFFERING FROM AURICULAR FIBRILLATION: OPERATION AND SURVIVAL.

By ANDREW EKLUND,
Nambour, Queensland.

Historical Survey and Ætiology.

MESENTERIC VASCULAR OCCLUSION was first recognized over a century ago, when Tiedman first reported it in 1843, and was followed by Virchow in 1847. Virchow again reported a case, and in 1854 published his report complete with full pathological findings in three cases. In 1904, Jackson, Porter and Quinby collected from the literature and published records of 214 cases. In 1913, Trotter made a further review of the literature and reported 360 known cases. In 1921, Loop reported that the condition had been demonstrated in 500 cases. Brown, in 1940, reported that the total had grown to 772, and that this series included all cases, whether arteries or veins or both had been occluded.

An analysis of the literature published indicates that the occurrence is rare. This rarity perhaps may be slightly exaggerated, because all writers stress the difficulty of making a diagnosis prior to surgical treatment or death. Many of the cases are reported from autopsy material. In one series of 367 cases collected from the literature, only 13 cases were correctly diagnosed prior to operation. In a period of seven years covering 30,000 admissions to an American hospital, only 13 cases could be collected, and four of these were recognized only at post-mortem examination.

Anything which interferes with the venous return of blood can be a cause of this condition. Intraabdominal infections, neoplasms and the surgical treatment for them (particularly when there is a tendency to cardiac decompensation), and degenerative arterial disease (arteriosclerosis, periarteritis and septic arteritis) are common causes, but the foremost cause, as every medical student knows, is auricular fibrillation with decompensation. It is the slowing of the blood flow which contributes to the occlusion in this type of case.

The incidence favours males in a ratio of two to one. It is commonest in persons aged over fifty years, but can occur at any age. As has already been gathered, the occlusion is in the superior mesenteric artery (61% of cases) and its companion vein (39% of cases). When the arteries only are affected, in 90% of cases the superior mesenteric artery is the site chosen; in the remainder the inferior mesenteric artery is affected.

When a vein is affected, thrombosis is the primary cause, and is nearly always due to some obstruction of the portal circulation. Other causes are a septic thrombosis originating from a septic focus, as in acute appendicitis, infected hæmorrhoids *et cetera*. In these cases the effects are usually less dramatic, the disease progressing only slowly, so that an opportunity is given for the development of a collateral circulation. On the other hand, when an artery is affected the effects are instantaneous and dramatic, the severity of the effects varying according to the level of the occlusion. When the main trunk of the superior mesenteric artery is affected, gangrene of the whole of the small bowel and the

large bowel as far as the transverse colon follows. The lower the level of the occlusion, the smaller the extent of the circulatory effects, and for a time at least the collateral circulation may keep the gut viable. Rapidly a secondary thrombosis sets in and spreads to all vessels distal to the site of the embolism, eventually reaching the terminal vessels of the bowel, which vessels have no collateral circulation. Unless operation is undertaken early, this secondary thrombosis can spread so far laterally that a far larger segment of bowel has to be resected than would have been the case if immediate operation had been undertaken.

In arriving at a diagnosis, the sudden occurrence of a severe shocking pain in the lower part of the abdomen in an elderly patient, particularly when signs of cardiac decompensation are also present and other phenomena of embolism are elicited, should immediately arouse suspicion of this vascular accident. The treatment is always surgical and entails the resection of the whole of the infarcted segment together with a reasonable margin of viable gut at either end. A good margin of healthy mesentery to include the thrombosed mesentery is removed. After closure of the blind ends a lateral anastomosis is performed.

Recovery has followed resection of the whole of the small intestine, and in other cases in which slightly smaller lengths have been removed, survival has occurred. The operative mortality is tremendous; it must be borne in mind that the condition occurs as a complication of another, and that the patient is a "bad surgical risk" in any case. Until 1940 the literature on the disease records approximately 100 operations with a total of 40 recoveries.

Clinical Record.

I had occasion to examine the patient first in April, 1951, when he complained of indigestion—a bloated sensation after certain foods. He had occasional blackouts then. His discomfort was relieved by taking baking soda. He was then aged sixty-nine years. He also complained at times of looseness of his bowels. On examination of the patient, I found nothing of importance other than a slow pulse with an occasional volume irregularity and an occasional extrasystolic pause. His condition settled down with a sedative and alkaline powder. I examined him again in May of that year, and apart from a note on his card to the effect that I thought his apex beat was displaced outward I made no further comment.

I did not examine him again till June 6, 1952. I was then called to his home at 11.20 a.m., and found him groaning with pain, hands clasped to the lower part of his abdomen; he was clammy-skinned and grey-faced. He told me that he had got up that morning to make the usual cup of tea at about 7.30 a.m. He then felt perfectly well. He had had his cup of tea and almost immediately had been seized with a severe pain which he first felt in the region of his navel. The pain was moderately severe at first and had gradually worsened. He stated that the pain had not varied in intensity except to grow worse, but after a while he noticed that the pain seemed to come more from the left side. He had not vomited, though he said that he felt as though he might at any time. He had a feeling of wanting to pass urine, but found difficulty in emptying his bladder completely. He said that he had had some difficulty with his micturition for some weeks previously. His main difficulty was in initiating the act.

On examination of the patient, there were present all the signs of severe shock. His blood pressure was unrecordable, because slow fibrillation was occurring. His heart size was increased. The chest was clear. The abdomen was slightly distended in all quarters. Tenderness was elicited over the whole of the lower part of the abdomen, the maximum tenderness being in the left iliac fossa and in the suprapubic area. Dulness to percussion was present over the whole of the lower part of the abdomen, and this dulness was constant in position. The bowel sounds were moderately loud. I gave him one quarter grain of morphine, and after he had picked up he was admitted to hospital.

My differential diagnosis at this stage was acute retention of urine, perforating diverticulitis, and lastly mesenteric vascular occlusion. His bladder was catheterized on his admission to hospital, 12 ounces of concentrated urine being withdrawn. There was little resistance to the passage of the catheter, and very little relief, if any, of his distress. The palpation of his abdomen at this stage revealed a doughy mass in his left iliac fossa extending into the loin. Palpation of this mass was not unduly painful (it must be remembered that he had had morphine previously). An enema was then given with a poor result. Rectal examination revealed a ballooned-out rectum, into which projected a moderately enlarged prostate gland. It was decided then to operate, and dextrose solution (4%) in 1/5 normal saline was given intravenously as a prelude to surgery. His condition did improve slowly over the next hour or two, and though uncomfortable and restless the patient was no longer in a state of shock.

At 5 p.m. the same day abdominal section under "open ether" anæsthesia was performed through a transverse incision at umbilical level, the left rectus muscle being divided transversely. When the peritoneum was reached, dark coils of bowel could be seen shining through the overlying peritoneum. As the peritoneum was opened, a moderate quantity of blood-stained fluid escaped, and approximately three feet of gangrenous small bowel (ileum) were quickly discovered. A fan-shaped area of swollen, friable mesentery radiated from a focal point in the vessel supplying the segment of bowel affected; this section of mesentery had a mottled, patchy, dark red appearance intermingled with patches which were almost black in colour. The bowel was quite unreacting, and it was decided to resect it together with the area of mesentery affected. Approximately four to six inches of healthy bowel were removed at either end of the affected segment, and a good margin of healthy mesentery surrounding the thrombosed area in the mesentery was also removed. The ends of the bowel were closed and a side-to-side anastomosis was performed about six inches from the blind proximal and distal ends, these ends pointing in the same direction. The mesenteric defect was closed by interrupted sutures. The abdomen was closed without drainage after a quantity of penicillin-sulphonamide powder had been applied to all sutured areas. A glove drain was used to drain the abdominal wall.

After operation, he was given "Distaquaine Fortified", 400,000 units twice daily, and the administration of digoxin added to his intravenous infusions was also begun. He was given 1·5 milligrammes of digoxin on the first day and 0·5 milligramme on succeeding days. A stomach tube was left *in situ* and was sucked out every two hours, a little saline being replaced after suction. Approximately three litres of dextrose solution (4% in 1/5 normal saline) were infused daily together with one litre of "Parenamine" per day. Daily requirements of vitamins *B* and *C* were added to the fluids given intravenously. After four days the patient commenced passing flatus. The heart action by the third post-operative day was normal and regular. Once the bowel sounds were clearly heard the stomach tube was removed and the administration of fluids by mouth was commenced. By the seventh post-operative day the intravenous therapy was able to be stopped. The abdominal wound healed cleanly by first intention, and the first bowel action occurred about the eighth day.

Complicating factors were mild post-operative pneumonia, which cleared up uneventfully, and retention of urine, which finally necessitated the insertion of an indwelling catheter. The patient had to be sent to the urological ward at the Brisbane Hospital because of this, but only after he had fully recovered from the operation. At this hospital he underwent a transurethral section of the middle lobe of his prostate. This procedure was complicated by a bladder hæmorrhage necessitating a blood transfusion. Upon his return home he required several weeks of supervision in his own home for persistent pyuria and mild pneumonia. From all this I am pleased to report that he recovered, and he is now well and able to lead a normal existence.

Summary.

A brief history of mesenteric vascular occlusion is given. The ætiological factors are briefly discussed.

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A case of mesenteric vascular occlusion in a patient, aged seventy years, is reported. The cause in this case was auricular fibrillation with a mesenteric embolus. Resection of the affected segment of bowel was performed with lateral anastomosis of the blind ends. After some minor complications the patient recovered and is now well.

Acknowledgements.

I wish to thank Dr. B. S. Skerman and Dr. A. S. Raine for their help at the initial operation. I wish also to thank Dr. E. P. Row for the urological work successfully performed. I should also like to thank the assistant librarian at the Brisbane Medical School Library for her assistance with the literature.

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Reviews.

Pathology in Surgery. By Edwin F. Hirsch, Ph.D., M.D.; 1953. Baltimore: The Williams and Wilkins Company. London: Baillière, Tindall and Cox; Sydney: Angus and Robertson, Limited. 9″ × 6¼″, pp. 492, with 388 illustrations. Price: $10.00.

PATHOLOGISTS in large hospitals have wide experience in the study of specimens of special interest in surgical pathology, and from time to time books are published on pathology which have a special interest from the surgical point of view. "Pathology in Surgery", by Edwin F. Hirsch, of Chicago, is such a book, arranged in eleven chapters, each concerned with one system of the body, and each provided with a short bibliography.

The work is an atlas rather than a text-book as usually understood, because, of the 474 pages, considerably more space is devoted to illustrations than to text.

The photographs of gross specimens are very good indeed and the photomicrographs are excellent; both cover a wide range. Two pages show eight gross specimens in colour; the remainder of the 388 figures are in black and white.

As the author states in the preface, the book is not a text-book in either general or special pathology, but he hopes that it will prove useful for pathologists, surgeons and surgical resident medical officers of the various specialties in hospitals and medical schools, and for medical students with some training in general pathology. The book does give valuable information on the gross and microscopic appearances of the lesions described, but the descriptions in the text are so brief that, in our opinion, an adequate understanding of these lesions will be attained only after additional study of other books on pathology. This is an inherent weakness of books like the one under review.

Prescription for Rebellion. By Robert Lindner; 1953. London: Victor Gollancz, Limited. 8″ × 5¼″, pp. 310. Price: 16s.

IN this book Lindner, himself a psychoanalyst, contends that psychology is being misapplied to such a degree that it may "send the species into the evolutionary shadows". Much of the blame can be traced to psychiatrists and psychoanalysts.

Man passes knowledge to others by ideas which may be either good or bad. One bad idea which may bring about the ruin of civilization, according to Lindner, is the idea that we must all adjust ourselves to a standard pattern of behaviour. Man has come to feel that if he can adjust his thinking and behaviour to the fixed pattern of our civilization he will achieve happiness. "You must adjust" has become another commandment.

Lindner claims that there is unanimous agreement among the institutions which guide us so that we should all be forced into the same mould. Psychiatric symptoms are in the form of a protest, but psychiatric treatment forces the patient to submit quietly to his subjection.

In this book all forms of psychiatric treatment are criticized, the shock therapists being referred to as "push button psychiatrists". The psychosurgeon is strongly condemned. The analyst is blamed for forcing the patient back into a rigid pattern of adjustment. Lindner claims that patients who have been psychoanalysed have the philosophy of submissive adjustment. He would prefer a philosophy of rebellion against the domination of our civilization.

The book is of interest to the psychiatrist in particular, as it shows clearly some of the weak points in psychiatric treatment.

Notes on Books, Current Journals and New Appliances.

Family Doctor. Published monthly by the proprietors, the British Medical Association, Tavistock Square, London, E.C.1. Sole agents for Australia and New Zealand: Gordon and Gotch (Australia) Limited. Subscription for twelve months: 20s. (sterling), including postage.

ONE of the great charms of *Family Doctor* is its abundant common sense. This finds expression in the August issue in articles on constipation, fashions, swimming, left-handedness, children who are larger than average, nature cures (the treatment of this subject is pungent), baldness and bringing up babies. Articles of general interest deal with the physiological effects of heat, the scientist and the sea, the embryology of the eye, and the almoner. Some aspects of suicide are discussed very thoughtfully. Intelligent housewives will find interest and help in articles on summer diet, on holiday housekeeping and on refrigerators. All the regular features have their usual place, and we are pleased to see that father is also given a place of his own with two pages of pictures, even though daughter Rosemary steals most of the thunder. This attractive magazine can be recommended by doctors to their patients with confidence. The wise doctor who buys it for his waiting room will need a double subscription unless he is prepared to let his patients wait till he and his family have read it, as they certainly will want to do.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Extrasystoles and Allied Arrhythmias", by David Scherf, M.D., F.A.C.P., and Adolf Schott, M.D. (Heidelberg), M.R.C.S.; 1953. London: William Heinemann (Medical Books), Limited. 10″ × 7½″, pp. 546, with 213 illustrations. Price: £5 5s.

The authors have endeavoured to give a description of the subject in its general biological context.

"The Sulphonamides and Antibiotics: In Man and Animals", by J. Stewart Lawrence, M.D. (Ed.), M.R.C.P., and John Francis, M.Sc., M.R.C.V.S., with the assistance of Arnold Sorsby, M.D., F.R.C.S., and Philip G. Scott, F.R.C.S.; Second Edition; 1953. London: H. K. Lewis and Company, Limited. 9″ × 6″, pp. 494, with 38 illustrations. Price: 42s.

The emphasis is chiefly on the clinical aspect and on the practical application of antibacterial agents to the control of natural infections.

"Compression Arthrodesis: Including Central Dislocation as a Principle in Hip Surgery", by John Charnley, F.R.C.S., with a chapter on Mechanics by Professor J. A. L. Matheson and Histological Observations by Professor S. L. Baker; 1953. Edinburgh and London: E. and S. Livingstone, Limited. 10″ × 7″, pp. 276, with 208 illustrations. Price: £2 2s.

The author holds that mechanical forces exist which can give to osseous union a purposeful direction to turn a random process into an orderly progress; these forces are found in strong mechanical compression.

"Isotopic Tracers in Biochemistry and Physiology", by Jacob Sacks, Ph.D., M.D.; First Edition; 1953. New York: Toronto and London: McGraw-Hill Book Company, Incorporated. 9″ × 6¼″, pp. 391, with 25 illustrations. Price: $8.50.

The purpose of this book is "to discuss the principles involved in the use of isotopic tracers, to describe the major accomplishments that have resulted from their application to biochemistry and physiology, and to point out some of the limitations inherent in their use".

The Medical Journal of Australia

SATURDAY, SEPTEMBER 12, 1953.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

LIND'S "A TREATISE OF THE SCURVY": A BICENTENARY.

IT is just two hundred years since the publication of the first edition of Lind's "A Treatise of the Scurvy". To mark this occasion the Edinburgh University Press has brought out a reprint of this work. Included in the book as "Additional Notes" are also "The Third Edition of the Treatise" by C. P. Stewart, "The Lind Tradition in the Royal Naval Medical Service" by Surgeon Vice-Admiral Sir Sheldon P. Dudley, "James Lind and Some of His Contemporaries" by D. Guthrie, "Scurvy in the Nineteenth Century and After" by C. P. Stewart, "The Chemistry of Vitamin C" by E. L. Hirst, and "The Role of Ascorbic Acid in the Human Body" by A. P. Meiklejohn, C. P. Stewart and R. Passmore.

During the last week in May of this year the Royal College of Physicians of Edinburgh and the Nutrition Society combined to hold a symposium to celebrate the bicentenary, and well-known workers from Europe and America presented papers on the present position of scurvy and ascorbic acid.[1] "Lind's Treatise of the Scurvy" is one of the great medical classics, and Sir Dudley Sheldon writes of it: "And, two hundred years after it was written, I am not competent to add a word to Lind's clinical account of the disease. For one reason, thanks to Lind himself, I have never seen a patient suffering from scurvy, despite the fact that for over forty years . . . I have been following his vocation of trying to improve the health of seamen." It took forty years for the British Admiralty to appreciate the value of Lind's work, but when they did the results were dramatic. In 1740 Commodore Anson left England with six fighting ships and two "victuallers" and over two thousand men to challenge Spanish supremacy in the Pacific. He returned after four years with only two hundred of the original crew; most of the rest had died of scurvy. This voyage was partly instrumental in stimulating Lind's investigations into scurvy. During the Seven Years War with France and Spain, when Lind was attached to the Royal Naval Hospital at Haslar, he usually had 300 to 400 patients suffering from scurvy under his daily charge in the hospital, and even 1000 at one time. Sir Gilbert Blane, a great naval physician and a contemporary of Lind, reported that "supplying lemon juice at Public Expense in 1795 acted so speedily that in less than two years afterwards it [scurvy] became extinct". Another sixty years had to pass before antiscorbutics were used in the mercantile marine, so firmly entrenched were false ideas about the nature of scurvy among civilian medical men.

Lind was essentially a "man of observation", as one of his pupils, Thomas Trotter, described him. He was one of the first, if not the first, of clinical observers in the modern style, and he had complete faith in the accuracy of his own observations and in the validity of his logical deductions from these observations. Without any of the modern trappings of research, he produced work which could hardly be bettered at the present day. This was not only in scurvy but also in malaria, typhus and general hygiene. He has been called the father of modern hygiene, although he got little recognition during his lifetime. His book, "A Treatise of the Scurvy", is a model for any clinical investigator, and could be studied with great advantage by all medical men, and particularly by those who wish to engage in clinical research. For a book written two hundred years ago, when medicine was wallowing in humbug and charlatanism, it is remarkably modern in its outlook, and is notable for the accuracy of the observations made and recorded, and for the logical deductions made from these observations. The book commences with "A critical history of the different accounts of this disease". Here is a critical summary of all the important work published on scurvy prior to Lind; it is very critical and no punches are pulled. It is a most interesting account of the gullibility and even dishonesty of physicians of the period. As a sample of his approach we may quote the following paragraph:

> The learned ignorance of that age lay concealed under a veil of unmeaning, unintelligible jargon. But in order to make way for the restoration of solid learning, it was found necessary to expunge all such terms as were contrived to give an air of wisdom to the imperfections of knowledge.

Of much that is published at the present time the same kind of remarks could well be made. For the first time Lind clearly distinguished the "occasional cause of the disease" (that is, the immediate cause) and the "predisposing causes" such as confinement, overwork, bad living conditions *et cetera*. One is reminded of Crandon's experiment, in which he lived for six months on a diet containing no vitamin *C* before developing any scorbutic symptoms, when one reads in a discussion on the predisposing causes in the tragedy of Anson's voyage: "While whole countries are observed to live on the same, nay, even a less wholesome diet; and many people for years abstain from vegetables, without almost any inconveniency." The value of fresh vegetables and fruit in preventing scurvy even in bad conditions is extraordinarily

[1] *Lancet*, June 20, 1953.

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well documented and it is difficult to see why the idea took so long to be accepted. Lind's approach may be seen in the following quotation:

> It being of the utmost consequence to guard against the first approaches of so dreadful an enemy, I shall here endeavour to lay down the measures proper to be taken for this end with that minuteness and accuracy which the importance of the subject, and the preservation of so many valuable and useful lives, justly demand; and at the same time shall, as much as possible, avoid offering anything that may be judged impracticable. . . . And lastly I shall propose nothing dictated by theory; but shall confirm all by experience and facts, the surest and most unerring guides.

Lind's chapter on "The Theory of the Scurvy" is of interest only because of the light it throws on the complete inadequacy of the physiological knowledge of the period to explain any bodily function. It was, indeed, not possible to determine the cause of scurvy before the "lucky accident", as it has been called, of Holst and Fröhlich in 1907 when they found, in some dietary experiments with guinea-pigs, the production of a condition which was clearly scurvy. In no laboratory animal, other than the primates, could scorbutic symptoms be produced and the way was now clear for experimental observations.

The following passages from the chapter "Of the Theory of the Scurvy" are worthy of reproduction:

> The best remedies are furnished from a composition of different plants, most eminent for the properties required: and whatever simple possesses the most of these qualities, is, of all such, the most serviceable and efficacious for preventing and curing the malady.
>
> It is to be remarked that, in most properties here requisite, vegetables differ from animal substances. That there is a considerable difference in the constituent principles of vegetables and animals is plainly proved by their chemical analysis. In the latter, the salts are found to be more volatile; and, by a great degree of fire, a volatile alcalescent salt is obtained from them: whereas a fixed alcaline salt is found copiously to abound in most vegetables when burnt; and indeed this last is properly of vegetable extraction.
>
> But, without this chemical torture, which shows so great a diversity in their component parts, many plants are of an acescent quality; whereas animal substances, on the contrary, are almost all of an alcalescent, or perhaps rather a putrescent nature. It would indeed appear that man, both from the structure of his organs of digestion and appetite, was designed to feed both on animal and vegetable substances. But though we perceive a person in health, and of a sound state of body, has a wonderful faculty of converting almost all sorts of alimentary substances into nourishment at times; yet experience shows that no man can long bear a diet entirely of flesh and fish without nauseating it, unless corrected by bread, salt, vinegar and acids; and that for the reason before observed, *viz.*, because the intention of digestion in the first passages is to draw from the aliment a milky, sweet, white liquor, resembling in quality a vegetable emulsion; not indeed acid, but acescent; contrary to the nature of animal substances, which are observed in like circumstances to become putrid. And for this and other reasons, a mixture of vegetable substances seems requisite towards the composition of good chyle, and to correct the continual putrescent tendency of the animal humours.
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> As animal digestion is a process *sui generis*, which no chemical operation has been found to imitate; none being able to convert food into chyle, or that into blood; all we can infer from experience is that in certain cases, as in the scurvy, vegetable juices and fruits of this tendency are found necessary to preserve health and life. If flesh, or animal substances, promote this process in the stomach, as would seem by some late experiments, we may from thence fairly conclude, flesh-soops stuffed with vegetables to be eminently antiscorbutic, which daily and incontestable experience sufficiently confirms.
>
> Upon the whole, it follows, and will be found true in fact, that the more any food, drink, herbs, or medicine, partake of any of the aforesaid qualities, the more antiscorbutic they become; but that the most perfect and effectual remedies are found in a composition of different ingredients, each possessing in a high degree one or other of those virtues, from the combination of which a vegetable, saponaceous, fermentable acid may result. Such an acid, ready prepared, is to be had in a certain degree in oranges, and most ripening sub-acid fruits; from whence they become the most effectual preservatives against this distemper.

In 1927 Szent-Györgyi isolated hexuronic acid from the adrenals and in 1932 he recognized that this was the factor which prevented and cured scurvy and renamed it ascorbic acid. The mode of action of ascorbic acid in the body is still unknown. Wolbach and his colleagues at Harvard from 1926 onwards showed that with deficiency of ascorbic acid there is a loss of collagen from connective tissues and a disappearance of intercellular cement. Formed collagen can be maintained, but new collagen is not adequately formed in the scorbutic animal. This fact explains all, or nearly all, the symptoms of scurvy, but the "biochemical lesion" responsible for this change is still unknown. The only other biochemical defect found in scurvy so far is in the oxidation of tyrosine. There is some evidence to suggest that ascorbic acid has something to do with the production of adrenocortical hormones and the adrenal cortex is one of the richest sources of ascorbic acid.

There is still no unanimity about the amount of ascorbic acid required by man. Most British authorities consider that 30 milligrammes per day are adequate; most American workers suggest a minimum of 75 milligrammes, an amount which, in all probability, most people in the world do not receive.

The meeting of the Royal College of Physicians of Edinburgh and the Nutrition Society closed with a dinner which included scurvy grass, adrenal cortices and paprika, all very rich sources of ascorbic acid and of historic interest in the investigations on scurvy.

Current Comment.

THE CAUSE OF ESSENTIAL HYPERTENSION.

THE elevation of the blood pressure in essential hypertension is due to vasoconstriction which is generally believed to be the consequence of over-activity of the sympathetic nervous system. The factors which bring about this over-activity are not known. Pericles Menof[1] has put forward a theory, and based it on what seems to be fairly good evidence, that in essential hypertension the normal blood pressure raising mechanism is not countered or is inadequately countered by the secretion of the thyroid gland. Sympathetic over-activity is equated with over-activity of the adrenal medulla. When Oliver and Schafer in 1894 were able to bring about a marked rise in blood pressure by injecting an extract of the adrenal medulla and later adrenaline was isolated and made synthetically and shown to have the same effect, it seemed that a mechanism for the elevation of the blood pressure had been demonstrated. Adrenaline, however, was very irregular in its action and search was made for another sympathetic activator or mediator and this has been shown to be l-noradrenaline, which is widely distributed in the body. Noradrenaline, then, is the factor responsible for the raised blood pressure in essential hypertension. There is considerable evidence that there is an hereditary factor in essential hypertension, but the nature of this is not known. Menof suggests that it is insufficiency of thyroid

[1] *South African M. J.*, May 16, 1953.

secretion. He bases this largely on the results he has obtained in the treatment of cases of essential hypertension with thyroid extract. He claims that in 229 of 334 cases, or about 70%, it was possible to bring down the blood pressure and to relieve the symptoms by the administration of thyroid extract. Oliver, as long ago as 1916, in his "Studies in Blood Pressure", observed that "ingestion of thyroid gland increases the calibre of the arteries and lowers the arterial pressure and in many cases of increased arterial pressure it is sometimes useful". Oliver also states that arterial pressure may be the resultant of the interaction of pressor and apressor products supplied by the blood. The observations seem to have been overlooked since.

Menof gives details of some experiments on the continuous infusion of l-noradrenaline solutions in man. The blood pressure rose from 120 and 90 millimetres of mercury (systolic and diastolic) to 200 and 130 millimetres. Three minutes after the infusion was stopped the blood pressure levels were 90 and 60 millimetres of mercury and this fall was associated with active flushing. In another experiment the subject developed a swelling of the thyroid gland which subsided half an hour after cessation of the infusion. In a woman patient with attacks of paroxysmal hypertension it was noted that when the attacks lasted longer than half an hour, enlargement of the thyroid gland occurred which subsided with the fall in blood pressure. Menof suggests that here and in the infusion experiments there is a temporary production of Graves's disease and that in Graves's disease the grossly excessive thyroid secretion, itself the result of noradrenaline excess, causes a reciprocal overaction of the adrenal medulla. Essential hypertension could be looked upon as Graves's disease where the thyroid gland has failed to put up a fight. Moreover, the fact that the thyroid has to fight at all instead of taking the challenge of the adrenal medulla, stimulated by emotion, suggests a weakness or insufficiency of the gland. Several observers have noted that essential hypertension is more common in persons who suffer, or previously have suffered, from Graves's disease.

Renal hypertension is the result of renal ischæmia and essential hypertension is the commonest cause of renal ischæmia. It follows that the majority of cases of essential hypertension will be complicated by varying degrees of renal hypertension so that, if the ideas of Menof as to the relation between the thyroid and adrenal medulla are correct, one must not expect from the thyroid treatment of hypertension uniformly favourable responses. In the light of these ideas one would expect thyroidectomy to be followed by hypertension, and there is some evidence that this is the case, but this wants further examination. The views expressed by Menof are interesting and may be very useful, but there is clearly need for much independent work before they can be accepted.

DRUG ADDICTION.

DRUG ADDICTION is a health problem in all parts of the world, in some countries much more than in others. In the United States it has been claimed, as a conservative estimate, that one in 3000 of the population is a drug addict, and recent investigations show an upward trend in addiction, the increase being predominantly among the younger members of urban populations. What the figures are for Australia we have no means of knowing, but the problem does exist to some extent. In view of the importance of the subject, *The American Journal of Medicine* has devoted its issue of May, 1953, to a symposium by specialists in particular branches of the subject. The articles published are as follows: "The Drug Addiction Problem', by J. M. Bobbitt; "Chemistry of Drugs of Addiction", by E. L. May; "Phenomena of Tolerance", by M. H. Seevers and L. A. Woods; "Clinical Characteristics of Addictions", by H. Isbell and W. M. White; "Psychiatric Aspects of Drug Addiction", by A. Wikler and R. W. Rasor; "Treatment of Drug Addiction", by H. F. Fraser and J. A. Grider, junior; "History and Mechanism of International and National Control of Drugs of Addiction", by A. Tennyson. As forty-eight pages are taken up by the articles a good deal of ground is covered.

Substances which have come to be regarded as addiction-producing are very diverse both in their chemical constitution and in their physiological effects. Whatever their chemistry, drugs which produce effects pleasurable to certain individuals may result in addiction. The majority of these drugs fall into three classifications: (*a*) morphine and its transformation products, (*b*) synthetic analgesics, and (c) sedatives and hypnotics. Most of the drugs in the first two groups have certain chemical features in common. The drugs of group (*c*), the barbiturates, have little or no chemical resemblance to the analgesic drugs but are more closely interrelated. Morphine is much the most widely used drug of addiction. Of the derivatives of morphine, heroin is the worst. It is a strong, fast-acting drug which rapidly gives rise to addiction and it is the drug of choice in the illicit drug traffic. As there are other drugs which will give much the same effects clinically as heroin and are less prone to abuse, the manufacture and sale of heroin are now prohibited in many countries, including Australia. Codeine, a much weaker analgesic agent, still has definite addiction liability, but much less than other members of the group. "Metopon" (methyldihydromorphinone) is a more potent analgesic than morphine with less pronounced drug addiction liability. Nearly all the synthetic analgesics with analgesic effects comparable with morphine have much the same addiction liability as morphine. Addiction to the barbiturates is common, is similar to chronic alcoholism, and is far more dangerous and harmful than is addiction to morphine or other analgesic drugs. The short-acting but potent "Nembutal", "Amytal" and "Seconal" are preferred by addicts to the milder, long-acting barbital and phenobarbital. Withdrawal of barbiturates from individuals chronically intoxicated with these drugs is followed by a very severe and definite type of abstinence syndrome. Addiction to paraldehyde and chloral hydrate is relatively uncommon. Other drugs, which do not fall into these groups, but which lead to addiction, are marihuana, cocaine, mescaline, and "Benzedrine" (amphetamine). There is no tolerance developed to these drugs nor are there true withdrawal symptoms. A feature of most of the drugs of addiction is the phenomenon of tolerance. By tolerance is meant the gradual decrease in the effect produced by repeated administration of the drug; or, conversely, a gradual increase in the dosage of the drug necessary to produce the same effect as did the initial dose. The first sign of tolerance to morphine and its allies is the shortening of the duration of the action following a given dose. Complaints are made that the drug is no longer effective. This is soon followed, especially if the dose is rapidly increased, or often repeated, by the disappearance of the narcotic effects of the drug, which include mental depression, malaise, muscular weakness, loss of appetite, sleepiness and analgesia. Tolerance is soon acquired to each new increment of the dosage. Almost complete tolerance has been developed to five grammes per day of morphine. Marked differences occur in the rate of development and the completeness of tolerance, and cross tolerances to different drugs may appear. The nature of the mechanisms involved in tolerance development is discussed at great length by Seevers and Woods, but the discussion is largely theoretical and does not lend itself to being summarized.

Other characteristics of addiction besides tolerance are seen clinically. With the opiates physical dependence and emotional dependence are of importance. Physical dependence refers to the development of an altered physiological state which requires continued administration of the drug to prevent the appearance of a characteristic illness, termed the "abstinence syndrome". Emotional dependence is a substitution of the use of the drug for other types of adaptive behaviour. In other words, use of the drug becomes the answer to all of life's problems. Addiction to morphine may be taken as representing addiction to any of the analgesic drugs. Proper therapeutic use of morphine is seldom followed by addiction, unless it is prolonged for good reasons. Most often addiction begins in the third

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decade of life but is not uncommon in teenagers. Experimentation with marihuana may precede experimentation with morphine or heroin. In the beginning the drug is usually taken either as snuff (heroin) or subcutaneously (morphine). The addict usually changes to intravenous administration. With increasing tolerance the need to obtain more drug leads to delinquency and illegal acts. The addict, after a brief period of increased activity, may drift into light sleep, suddenly awaken and drift back to sleep. It is in this period that dreams occur, but these dreams are identical with the normal fantasies of the individual; the drug merely facilitates indulgence in fantasy. Intravenous injection of morphine produces dramatic effects. Within a few seconds there is sudden dizziness, flushing and itching. The effects are said to resemble those of a sexual orgasm. With heroin the flushing and itching are not experienced and this is one of the reasons for the preference shown for heroin by many addicts. These effects pass after a few minutes and the symptoms are then like those following subcutaneous injection. With increase in tolerance the addict can usually carry on highly technical work fairly satisfactorily provided he can get sufficient of the drug. There is, however, marked diminution in sexual activity. Severe symptoms follow withdrawal of the drug. There are extreme restlessness, twitching, sleeplessness and later retching, vomiting and diarrhœa. The subject eats and drinks little and rapidly loses weight. The symptoms reach peak intensity forty-eight hours after the last dose of morphine, then decline for seven to ten days, when most of them have disappeared. A sufficiently large dose of morphine abolishes symptoms within a few minutes, and the change from an ill, miserable, dishevelled individual to a clean and cheerful individual within 30 minutes is dramatic. Addiction to barbiturates does not ordinarily occur unless the patient is consuming 0·8 gramme (eight grains) or more of a potent, quick-acting barbiturate daily. Addiction to alcohol or opiates is frequently involved in the genesis of barbiturate addiction and very commonly there is mixed addiction, barbiturates with alcohol and amphetamine being very common. Intoxication with barbiturates resembles intoxication with alcohol. Tolerance to barbiturates is never complete, and for this reason acute poisoning may occur in a chronically intoxicated individual. Very severe symptoms may occur after the withdrawal of the drug. These are somewhat like those following removal of morphine in morphine addicts, but violent convulsions and delirium may occur. With cocaine addiction there is an ecstatic sensation of extreme physical and mental power with loss of sensation of fatigue and hunger, but these effects last only a few minutes so there is repetition of the dose at frequent intervals. As the dose is increased toxic symptoms appear. A characteristic toxic psychosis, with paranoid delusions, usually develops. Tolerance to cocaine does not develop, rather increased sensitivity to the effects of the drug, and there are no true withdrawal symptoms. Cocaine is almost always used in conjunction with morphine or heroin. Symptoms of intoxication with the sympathomimetic amines ("Benzedrine", d-amphetamine *et cetera*) resemble those of intoxication with cocaine. The symptoms develop more slowly but last longer. Tolerance is not usual but some addicts are known to take as much as 2000 milligrammes of amphetamine daily. These drugs are seldom taken alone, but usually with barbiturates or alcohol. Marihuana is usually smoked. The subjective effects include elation, great amusement at simple jokes, and distortions of time and space perception. Toxic psychoses may occur. There is very little tolerance developed and there is no abstinence syndrome.

As regards treatment of drug addicts, it is pointed out that this is primarily a psychiatric problem and favourable results cannot be anticipated unless treatment has been continued for several months. Attempts to carry out such therapy in the home fail almost invariably. Psychiatric success is difficult to evaluate and actual cure is regarded by some as unobtainable. Nevertheless many patients may be helped. Since 1909 many attempts have been made to get international agreement about the production and sale of drugs of addiction, with fair success in the sense that there has been drastic reduction in the production of these dangerous drugs. Smuggling and illicit selling are, however, still very prevalent. It is to be noted that the barbiturates and other somnifacient drugs are not included in the present system of international control, although their purchase is controlled in some countries.

CATION EXCHANGE RESINS AND ANTIBIOTICS.

CATION exchange resins have found an accepted, if limited, place in therapeutics in the reduction of œdema. However, the very properties on which their therapeutic value depends are potential sources of difficulty. They reduce œdema by removing sodium from the body, but, as I. S. Friedman, S. Zuckerman and E. McCatty[1] point out, they are not individually selective; they combine with any substance which has a positive charge or which is amphoteric. In addition to cations they are known to absorb thiamin, riboflavine and alkaloids (quinine, atropine, scopolamine), and it is obvious that a knowledge of their effect on other therapeutic substances is important. The problem presented to Friedman, Zuckerman and McCatty arose in relation to a patient suffering from congestive cardiac failure who was being successfully treated with an exchange resin; she developed atypical pneumonitis, and the effect of the exchange resin on antibiotic therapy was called in question. The method of investigation was to determine in the laboratory the growth inhibition of four known organisms by the common antibiotics and to note any differences when a cation exchange resin was added. It was found that the resin alone did not inhibit the growth of any of the organisms. Each of the antibiotics used alone produced a significant zone of inhibition of growth of normally susceptible organisms. Penicillin or chloramphenicol combined with a cation exchange resin had the same inhibitory effect as when used alone. Dihydrostreptomycin, when combined with the resin, lost its antibacterial activity immediately for both Gram-positive and Gram-negative organisms. Terramycin and aureomycin when combined with the exchange resin were inactivated immediately for Gram-negative organisms and within five hours for Gram-positive organisms as well. It is clear that the results obtained could not be attributed to variations in pH produced by the resins, but that dihydrostreptomycin, terramycin and aureomycin are absorbed by the resins and their antibacterial activities are suppressed. The activity of penicillin and chloramphenicol is not affected. The implications of these findings in relation to oral antibiotic therapy should be apparent.

TREATMENT OF PURULENT MENINGITIS OF UNKNOWN ORIGIN.

PERHAPS one of the most acute medical emergencies that can occur in hospital or in general practice is to encounter a child with acute purulent meningitis. It is true that, with the advent of so many antibacterial agents, meningitis has lost much of its terror; but prompt treatment is necessary and one must have a clear and satisfactory plan of attack. Mark Lepper[2] and his associates have endeavoured to lay down rules for treatment, based on their experience at the Municipal Contagious Diseases Hospital, Chicago. Over a two-year period 246 patients with purulent meningitis were treated at this hospital. In 130 cases the meningococcus was the causal agent, in 24 the pneumococcus, in 34 *Hæmophilus influenzæ*. The results of treatment in these groups have been reported previously.[3,4,5] In 21 cases other bacteria (excluding *Mycobacterium tuberculosis*) were isolated; in 37 patients the causal agent could

[1] *Am. J. M. Sc.*, April, 1953.
[2] *Am. J. Dis. Child.*, March, 1953.
[3] *Arch. Int. Med.*, October, 1951.
[4] *Am. J. Dis. Child.*, June, 1952.
[5] *J. Lab. & Clin. Med.*, December, 1952.

not be demonstrated, but 17 of these were well on the way to recovery before admission. The preesnt study deals with these two groups, excluding the 17 patients who were recovering when admitted to hospital.

In the first group the causal agents were as follows: β-hæmolytic streptococcus (six cases), α-hæmolytic streptococcus (two cases), *Staphylococcus pyogenes* (three cases), *Klebsiella pneumoniæ* (two cases), *Listeria* (one case), *Escherichia coli* (four cases, in one of which the pneumococcus was grown also), *B. alkaligenes* (one case), *Pseudomonas* (one case) and *Corynebacterium* (one case).

In the treatment of meningitis of known origin penicillin is probably the best therapeutic agent for pneumococcus infections and satisfactory for most Gram-positive cocci, with the possible exception of staphylococcus infections, in which the variable picture of sensitivity makes the choice of a drug most difficult. In influenza bacillus infections it would seem likely that aureomycin or chloramphenicol or tetramycin is suitable. In meningococcus infections the problem is simple, for penicillin in adequate dosage proved as effective as sulphonamides; and aureomycin, oxytetracycline (terramycin) and chloramphenicol seem effective, though they have not been used extensively for this infection. As to the other Gram-negative rod infections all the latter antibiotics are suitable, with chloramphenicol perhaps the choice in Friedländer's infection. Polymyxin may be tried when others fail.

In the diagnosis of meningitis expert pathological assistance is essential. A smear of the spinal fluid should be used as a guide for treatment, and if the organism is demonstrable a provisional diagnosis can be made and appropriate treatment instituted. Culture may confirm, alter or amplify the provisional diagnosis, and sensitivity tests provide additional information. In only seven of the 41 cases in this study was the diagnosis possible by examination of a smear of the initial spinal fluid. Further, 8·5%, 12·5% and 14·7% of the meningococcus, pneumococcus and hæmophilus patients respectively had initial smears "negative" for pathogens, so that in 70 of the 246 patients it was impossible to make a specific ætiological diagnosis before treatment was commenced, and in 37 of them a cause was never established.

Even with the best of laboratory facilities it will sometimes happen that one is confronted with a case of purulent meningitis in which no organisms can be demonstrated. Lepper and his asociates advise that two criteria should govern the choice of drug: (*a*) the age of the patient and (*b*) the degree of illness. In the age group under ten years the most common organism is *Hæmophilus influenzæ*, so that one of the antibiotics generally used in these infections should be selected. However, if the child is critically ill and there is good reason to suspect a pneumococcus infection, such as an accompanying pneumonia, penicillin should be used and streptomycin may be added. According to these American workers, in the age group over ten, and particularly the older ages, the pneumococcus is by far the most serious offender. It is doubtful whether this is the case in Australia. They recommend that if the patient is only moderately ill, penicillin alone is sufficient, but if he is critically ill, streptomycin can be added in case a Gram-negative rod is involved. Meningococcus infections respond well to many different agents. It is often stated in text-books that where no organisms can be found, the meningococcus is the most likely offender. In patients with the Waterhouse-Friderichsen syndrome the meningococcus can usually be demonstrated; in any case these patients are so ill that the diagnosis must be made on clinical grounds and made immediately.

IS INFLAMMATION BENEFICIAL?

THE action of a large variety of different agents on tissue cells brings about the series of changes in the tissue called inflammation. The common factor is that the agents kill tissue cells. There is a regular sequence of events following the destruction of the cells. First there is exudation of plasma from the capillaries which are dilated and fibrin forms locally. There is increasing dilatation of blood vessels around the site of injury. Massive leucocyte migration then takes place; there is much œdema with fibrin formation. There is evidence that from the damaged cells are produced diffusible substances which bring about the exudation of fluid and the vascular phenomena of inflammation. Histamine, the H substance of Lewis, and peptides from the partial digestion of proteins are such diffusible substances. How these substances are produced is not known for certain, but a tryptic digest of blood albumin and other proteins has similar properties. A crystalline peptide, from digestion of fibrin, with a molecular weight of about 6000, has been isolated which increases capillary permeability, causes vascular endothelium to swell, and induces leucocytic migration from the blood vessels. It is possible that proteolytic enzymes, set free when cells are killed, bring about the production of such peptides and also histamine. The usual teaching about inflammation is somewhat as follows. As the result of injury to cells due to many kinds of agents a diffusible substance or substances is set free rapidly and diffuses into tissue spaces. These cause dilatation of the arterioles and venules of the area surrounding the damaged cells and increased permeability of the capillaries. The blood flow is first increased, later slowed, plasma escapes from the capillaries and somewhat later leucocytes also. The fluid exuding into the tissue spaces dilutes the injurious agent and the products of its action and washes these away. Clotting of the exuded plasma produces a fibrinous gel which fills up many of the crevasses and lymphatics and prevents dispersion of the injurious agent, particularly bacteria. Migration of leucocytes is also a protective device, for it results in the collection of masses of phagocytes where they are most needed. G. R. Cameron[1] asks whether this story is true and whether inflammation is really beneficial.

Exudation of fluid is said to dilute harmful material provided means exist for the removal of the fluid. But this may spread the injurious material over a much wider area. This can be particularly important with virulent bacteria. The blocking of pathways from the inflamed area by fibrin from the clotting of the exuded plasma is said to be of advantage. But fibrin forms an excellent medium for the growth of many bacteria which produce inflammation. In any case the production of fibrin is slow in developing and is often delayed until too late to hold up the spread of bacteria. The presence of fibrin thrombi in the lymphatics of the inflamed area is said to reduce the flow of lymph from the area. But direct measurements have shown that there is increased flow of lymph. In spite of all that has been claimed about the value of phagocytosis by leucocytes, there is no convincing evidence of the value of phagocytosis in living tissues, especially against large numbers of bacteria or against virulent strains of bacteria. A great deal of experimental evidence has shown that during the early stages of inflammation the affected tissue is no more resistant to the absorption of bacteria than normal tissue. The time required for an effective amount of inflammation to develop about invasive bacteria is much longer than the time required for bacteria to spread. "Only when the exudate contains specific antibodies against the invaders do we find convincing evidence for the view that inflammation is protective in function." In other circumstances inflammation may be a nuisance or a menace. "It is a kind of evolutionary gloss, a blundering, clumsy affair which can add to the burden of the already overtaxed organism but which may turn out to be an advantage if the organism has already learnt the trick of providing the most successful of all safeguards, immune bodies."

[1] "Lectures on the Scientific Basis of Medicine", British Postgraduate Medical Federation, University of London; 1953. Volume I, 1951-52. London: University of London: The Athlone Press. Sydney: Walter Standish and Sons. 9" × 6", pp. 404, with six plates and 85 text figures. Price: 30s.

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Abstracts from Medical Literature.

PHYSIOLOGY.

The Small Intestine as a Factor in Regulation of Eating.

R. G. HILL, E. C. ISON, W. W. JONES, AND J. W. ARCHDEACON (*Am. J. Physiol.*, July, 1952) report that Maydl fistulæ were established in dogs. Solutions containing a sufficient quantity of glucose in hypertonic solution were effective in limiting food intake as determined by free selection of a standard food supply. Experiments with a non-nutritive fibre lend weight to the postulate that fullness, distension or muscular activity of the intestine, or a combination of these, does initiate reflexes which at least temporarily dull the desire to eat. However, whatever degree of inhibition may be exerted, it does not seem to be of great magnitude. Tyrosine was not effective in inhibiting intake, as measured in these experiments.

Experimental Production of Leucopenia in Rats by Thyroid Feeding.

J. G. PALMER, G. E. CARTWRIGHT, AND M. M. WINTROBE (*Am. J. Physiol.*, November, 1952) report that rats fed desiccated thyroid and a diet limited in caloric value developed severe leucopenia and lost weight. The leucopenia involved both granulocytes and mononuclear cells and was not accompanied by anæmia. It was not corrected by increasing any one of the constituents of the diet or by giving vitamin B_{12}, folic acid, citrovorum factor, ascorbic acid, lyxoflavin, whole liver powder, vegetable fat or yeast. Evidence is presented which suggests that the leucopenia is related to a limited caloric intake.

Changes in Flicker Fusion Frequency under Stress.

J. BROZEK, E. SIMONSON, AND H. L. TAYLOR (*J. Appl. Physiol.*, January, 1953) report that within a framework of studies on changes in quantitative criteria of "fitness" the flicker fusion frequency (FFF) was determined during a control period and under the following conditions: (i) A day's work in library and laboratory jobs judged to involve a moderate amount of visual strain (FFF decrement of less than 0·5 cycle, statistical significance questionable). (ii) Two hours of strenuous visual work under varied conditions of illumination (consistent decrement of about one cycle; no significant relationship to the work stress gauged by the level of illumination and the performance decrement after two hours of work). (iii) Nutritional stresses—starvation, prolonged semistarvation and thiamine deficiency (small decrements which reached the level of statistical significance after six months of semistarvation with a decrement of one cycle, and after three days of acute starvation with a decrement of 1·6 cycles); addition of hard physical work reduced rather than increased the decrement. (iv) Miscellaneous severe stresses—hard physical work, work in hot environment and loss of sleep for two nights (no statistically significant change). The mechanism involved in the depression of fusion level in situations in which such a change has been demonstrated (starvation, strenuous visual work) is not clear, and most likely it varies. The authors state that from the results presented in this paper it seems clear that the decrease of the fusion level cannot serve as an index of the degree of involvement of the central nervous system in biological stresses of the type applied in this study or that this involvement is minimal.

Ineffectiveness of Artificial Respiration in Rats after Drowning.

H. E. SWANN, JUNIOR, P. V. KARPOVICH, AND D. B. DILL (*J. Appl. Physiol.*, February, 1953) state that Fainer *et alii* in a recent paper concluded that artificial respiration, manual and mechanical, was ineffective in reviving dogs after drowning. The chances of survival according to their findings were equal whether the animals were subjected to artificial respiration or not; they offered a tentative explanation that this ineffectiveness was not caused by obstruction of the airways but was due to death from ventricular fibrillation. The present authors report that 30 white rats were submerged in fresh water until the end of struggle, after which they were removed from the water. Of 15 rats not given artificial respiration, five revived. Of 15 other rats given artificial respiration, four revived. Of 18 rats which did not revive, in only two did the heart stop beating within six minutes after removal of the rat from water, while in the remaining 16 the heart continued to contract for six to eight minutes. No ventricular fibrillation was observed. Examination of the lungs showed that the main difference between rats which did and did not revive was that while the former had tracheæ filled with water and foam, in the latter they were free from obstruction. Artificial respiration had no beneficial effect, and its failure was apparently caused by blocking of the airways by water and foam.

Action of Salicylates and Related Drugs on Inflammation.

G. UNGAR, E. DAMGAARD, AND F. P. HUMMEL (*Am. J. Physiol.*, December, 1952) report a method for the evaluation of the anti-inflammatory action exerted by salicylate and related drugs. Results obtained by this method are consistent with clinically observed effects of these drugs. Although salicylate does stimulate the pituitary-adrenocortical system, it cannot inhibit inflammation by this mechanism, since its action is not prevented by hypophysectomy or adrenalectomy. The anti-inflammatory action of the drugs studied may be explained by the fact that they inhibit fibrinolysin, an enzyme which probably plays a role in the mechanism of inflammation. A satisfactory parallelism was observed between the in-vivo anti-inflammatory action and the in-vitro fibrinolysin inhibition. The concentrations of salicylate which inhibit fibrinolysin *in vitro* are of the same order as the blood levels required for the in-vivo pharmacological action.

Lean Body Mass as a Metabolic Reference Standard.

A. T. METLER, JUNIOR, AND C. S. BLYTH (*J. Appl. Physiol.*, January, 1953) report that basal oxygen consumption, body fat and lean body mass, plasma protein-bound iodine content and plasma cholesterol content were measured in 48 college students, with a body fat range of 2·7% to 44·0% and a lean body mass range of 40 to 91 kilograms. Thyroid status, as measured by the plasma protein-bound iodine level, was normal in all the subjects. The best metabolic reference standard was found to be the lean body mass (correlation equals 0·92). It is pointed out that other standards, such as surface area and body weight, may derive much of their validity from their correlation with lean body mass. From the linear regression equation relating basal oxygen consumption and lean body mass, oxygen consumption per minute may be predicted within ± 31 and ± 32 millilitres, respectively. The influence of varying body fat content on the calculated metabolic rate based on both lean body mass and surface area is discussed.

A Study of the Eosinophile Cell Response to Exercise in Man.

R. F. WAKE, B. F. GRAHAM, AND S. D. MCGRATH (*J. Aviation Med.*, April, 1953) report that 21 healthy males were exercised in a gymnasium for twelve hours from 8 a.m. to 8 p.m. On another day they were rested for a similar period. On each occasion eosinophile cell counts were obtained every two hours. Statistical evaluation of the data indicated that the counts, other than the first and second, were significantly lower on the day of exercise. It may be concluded that exercise of this order causes activation of the adrenal cortex.

BIOCHEMISTRY.

Cortisone.

J. H. BALMAIN AND S. J. FOLLEY (*Arch. Biochem.*, July, 1952) have shown that cortisone exerted strong effects *in vitro* on the respiration of mammary gland slices from twenty-day-pregnant rats. These effects appear to be such as would be expected if secretory changes had been initiated. On the other hand, the tissue was inert to prolactin at this stage. Conversely, the respiration of tissue taken during the first five days of lactation was sensitive in a similar way to prolactin but inert to cortisone.

I. CLARK (*J. Biol. Chem.*, January, 1952) has presented evidence that cortisone causes an increase in urinary nitrogen content because it acts as an inhibitor or regulator of protein synthesis. The validity of using urinary nitrogen data for calculating the status of protein synthesis in the rat has been confirmed by tissue analyses. It is suggested that, during cortisone treatment, the liver acts as a detoxicating agent by preventing the accumulation of nitrogenous substances not elsewhere utilized by the body. Evidence is presented that increased anabolic activity of an organ is accompanied by an increase in its non-protein nitrogen. Also, increased catabolic activity of an organ is characterized by a decrease in its non-protein nitrogen.

Ascorbic Acid.

R. R. SEALOCK *et alii* (*J. Biol. Chem.*, June, 1952) have carried out analyses for both free and bound ascorbic acid in liver tissue from scorbutic guinea-pigs and have shown that a sufficient quantity of the vitamin is present to oxidize the amino acid tyrosine when relatively large amounts of tissue are

employed. A dialysed extract, prepared from acetone-powdered guinea-pig livers, completely oxidizes tyrosine when α-keto-glutaric acid and ascorbic acid are added to the system. The ascorbic acid is added in catalytic amounts, a final concentration of approximately 0·0005 M being necessary for the maximal rate of the reaction. The same type of extract also oxidizes the tyrosine keto acid when the vitamin is added. It is concluded that ascorbic acid acts as a coenzyme in tyrosine oxidation.

Folic Acid.

G. TOENNIES *et alii* (*J. Biol. Chem.*, January, 1953) have shown that dialysates prepared from blood hæmolysates at low temperature show folic acid activities measured by *Lactobacillus casei*, which are 20 to 100 times as high as those previously reported for human blood. The active factor (or factors) is subject to changes on storage of the dialysates at 2° C., an initial phase of increase being followed by loss of activity.

Erythrocytes.

W. L. MORRISON AND H. NEURATH (*J. Biol. Chem.*, January, 1953) have established the presence of three proteinases in crude stroma suspensions of lysed human erythrocytes. One has maximum activity at pH 7·4 and is activated by reducing agents as well as zinc and ferrous ions; another is maximally active at pH 7·4, is activated by zinc and ferrous ions but not by reducing agents; the third has maximum activity at pH 3·2 and fails to be activated by reducing agents or metal ions.

ACTH.

S. ROBERTS (*J. Biol. Chem.*, January, 1953) has reported that the release of protein to a serum medium by rat liver and splenic tissue *in vitro* was enhanced by previous treatment of the animals with adrenal cortical extract or ACTH. Adrenalectomy depressed the rate of protein release. The protein released by the liver tissue possessed the electrophoretic mobility of serum α-globulin; that released by the spleen was similar to serum β-globulin. Disappearance of albumin from the serum medium was coincident with the addition of globulin. The results indicate that the primary effect of the adrenal cortical secretions on nitrogenous metabolism involves accelerated mobilization of protein. This action appears to be effected by labilization of tissue protein and the resulting translocation of this protein to other sites in the body in the form of specific plasma proteins.

Von Gierke's Disease.

G. T. AND C. F. CORI (*J. Biol. Chem.*, December, 1952) have measured the glucose-6-phosphatase activity in liver homogenates from six subjects of glycogen storage disease. In two fatal cases the enzyme was practically absent; this could not be explained by the presence of an inhibitor or by the lack of cofactors. The activity of the acid phosphatase at pH 5·0, and of the alkaline phosphatase at pH 9·0, with glycerophosphate as substrate, was not appreciably diminished. Owing to the absence of the specific phosphatase which has its optimum at pH 6·8, it could be shown that the unspecific phosphatases had practically no action on glucose-6-phosphate in the physiological pH range. The phosphoglucomutase reaction was not rate-limiting, since glucose-6-phosphate accumulated when glucose-1-phosphate was added to the homogenates. In two out of four surviving subjects of von Gierke's disease with mild symptoms the activity of the specific phosphatase was below the level found in other liver diseases.

B. ILLINGWORTH AND G. T. CORI (*ibidem*) studied the liver glycogen from 10 children with von Gierke's disease, and in eight of the ten instances no abnormality of glycogen structure could be detected. In one case, in which both liver and muscles were involved, the liver glycogen had very short outer branches and the muscle glycogen had almost none, resembling a phosphorylase limit dextrin. In another case the liver glycogen was less branched and had longer inner and outer chains than normal glycogen. The authors state that these two cases point to different kinds of enzymatic deficiency and emphasize the fact that there are different types of glycogen storage disease.

Cholesterol.

S. O. BYERS AND M. W. BIGGS (*Arch. Biochem.*, August, 1952) have administered trituum-labelled cholic acid to the rat with bile-duct obstruction. The examination of the body cholesterol revealed no evidence for conversion of cholic acid to cholesterol. The conversion of cholesterol to cholic acid was confirmed. The mechanism by which excess cholic acid produces excess hypercholesteræmia in rats with biliary obstruction does not involve conversion of cholic acid to cholesterol.

R. G. LANGDON AND K. BLOCH (*J. Biol. Chem.*, January, 1953) have prepared C^{14}-squalene biosynthetically from acetate and shown that it is efficiently converted to cholesterol in the tissues of the mouse. This adds to the evidence that squalene is normally an intermediate in the synthesis of cholesterol.

G. M. TOMKINS *et alii* (*ibidem*, December, 1952) have studied the incorporation of acetate into cholesterol in liver slices prepared from normal and from hypophysectomized rats. Hepatic cholesterogenesis was greatly reduced in the hypophysectomized rat.

Amino Acids.

E. V. FLOCK *et alii* (*J. Biol. Chem.*, February, 1953) have reported that characteristic changes appear in the brain as a result of loss of hepatic function. The concentration of free amino acids of the brain increases progressively up to approximately twice the normal value in from thirteen to twenty-four hours after total hepatectomy in the dog. This is preponderantly due to the five-fold increase in the amount of glutamine. There is, however, no significant change in the concentration of glutamic acid. A definite but smaller increase in the concentration of glutamine in muscle also occurs, but this is associated with a decrease of similar degree in the concentration of glutamic acid.

Testosterone.

J. ASHMORE *et alii* (*J. Biol. Chem.*, February, 1953) reported the synthesis of testosterone 4-C^{14}. When it was administered to normal animals, approximately one-third of the administered radioactive substance was excreted in the urine and two-thirds in the fæces. In animals with cannulated bile ducts it was found that the bile served as the major route of excretion, while in animals with ligated bile ducts the kidney served as the major pathway of excretion. Significant amounts of the compounds excreted in the bile were resorbed from the intestinal tract when bile containing radio-metabolites was administered to other bile fistula animals. No radioactivity was found in the expired air. Hydrolytic studies indicated that the radio-metabolites in the fæces were different from those in the bile.

Trituum.

R. C. THOMPSON (*J. Biol. Chem.*, February, 1953) has administered trituum oxide intraperitoneally to 40 rats. The animals were sacrificed at intervals after administration, and trituum of body water and tissue-bound trituum were determined in various organ and tissue samples. The biological half-life of body water in the rat was found to be 3·3 days. All organs and tissues sampled (except blood) contain components which lose tissue-bound trituum with a biological half life of eighty days or longer. Evidence is presented which suggests strongly that these long-lived components represent a significant proportion of the total animal tissue.

Calcification.

V. DISTEFANO AND W. F. NEUMAN (*J. Biol. Chem.*, February, 1953) have used radio-calcium and ion exchange resins to demonstrate conclusively that calcium forms relatively undissociated complex ions with ATP and ADP. It has been shown that the phosphatases present in rhachitic bone cartilage liberate only small amounts of inorganic phosphorus from ATP. These results explain the inhibitory effect of ATP on calcification *in vitro*.

Adaptation.

M. W. GORDON AND M. RODER (*J. Biol. Chem.*, February, 1953) have shown that fertile chick embryos are capable of elaborating adenosine deaminase in response to injections of adenosine during various stages in the development of the embryo. The response is greater when the injections are given over a period of days rather than in a single dose.

Steroids.

H. ROSENKRANTZ (*Arch. Biochem.*, May, 1953) has found that solutions of antimony trichloride in nitrobenzene gave characteristic colours with 51 steroids. The reagent afforded a simple procedure for detecting hydroxy steroids on paper chromatograms, and had a sensitivity of approximately 1·5 micrograms per square centimetre. Several pairs of steroids have been differentiated in single migrating zones on the basis of colour differences. It has been demonstrated that a forty-eight hour chromatogram using a toluene-propylene glycol system permits resolution of a pure mixture of œstriol, œstrone, α-œstradiol and β-œstradiol.

Ergosterol.

D. J. HANAHAN AND S. J. WAKIL (*Archiv. Biochem.*, May, 1953) have shown that from 2% to 5% of ergosterol-C^{14} administered orally is absorbed within six hours, mainly via the lymph system. The bile represents a major excretory pathway for the metabolites of this compound. None of the radioactivity present in the bile could be identified as ergosterol.

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Special Articles for the Clinician.

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LXXIX.

PINK DISEASE.

THE syndrome recognized as pink disease is perhaps one of the most difficult problems in pædiatrics as far as diagnosis is concerned. Once diagnosed it is an extremely difficult condition to treat, and even during the course of treatment it is equally difficult to foretell the ultimate outcome in any particular baby.

The diagnosis is difficult mainly because the onset, in the great majority of patients, is insidious and variable in character, and there is no single laboratory test available which will confirm a clinical suspicion. The treatment is difficult and unsatisfactory mainly because the underlying cause of the condition is at present unknown.

The prognosis is always a matter of uncertainty because with the baby suffering from pink disease, as with cricket, one never knows from day to day, even from hour to hour, just what may happen next.

Pink disease may be regarded for clinical purposes as being restricted to infants and toddlers between the ages of six and twenty-four months. This corresponds to the period of the first dentition, and for this reason many of the infants in the incipient stage of the disease are regarded as suffering from "teething troubles"—that "dangerous diaper for draping diagnostic doubts".

The age incidence reaches its peak in the eighth, ninth and tenth months of life. A few babies are involved as early as the age of three months, and at the other extreme are a few older children aged up to three or four years; quite exceptionally in this country it has been recorded in adults.

Clinical Manifestations.

The clinical manifestations will be discussed as follows.

Weight.—Failure to gain weight, or even a slight loss of weight in an infant who has previously been progressing satisfactorily, is one of the earliest indications that all is not well with this particular baby.

Irritability.—A change in temperament becomes evident, and the baby, previously happy and contented, becomes irritable and "grizzly", cries continually in a whining or howling manner, and may be noticed to hold his ears or bang the head as if in pain. Rarely a convulsive seizure occurs at the onset, and the infant seems tender on handling, and wants to be kept moving in the pram or soaking in a warm bath. Whatever the particular manifestation of this irritable state one may be sure that it will persist and become progressively worse for weeks or months, during which period the infant is never known to smile. The picture is one of abject misery unsurpassed by any other clinical condition in babies of this age group. The lessening of the irritability and the return of an occasional smile are the early indications of a slight improvement.

Photophobia.—Often the baby is noticed to be frowning, holding his hands over his eyes, especially if in bright sunlight, or burying his face into the pillow or onto the shoulder of the mother when she is carrying him. Sometimes there is considerable injection of the conjunctivæ, with profuse lachrymation and a watery discharge which lasts for some days but rarely becomes purulent. On occasions the infant "gropes" round almost as if he were blinded. These manifestations are all indications of the intense dislike for bright light which is so characteristic of the disease.

Weakness and Hypotonia.—Weakness and hypotonia are present in all babies with pink disease and in some are so intense as to simulate an early poliomyelitis infection. A baby who was previously walking or crawling is described by the mother as "having gone off his feet", and is content to lie curled up in the one position for considerable periods, even to such an extent that trophic lesions appear about the extremities and may be followed eventually by deformities of the fingers or toes. The hypotonicity may result in the appearance of inguinal or umbilical herniæ or in the frequent occurrence of rectal prolapse. When the condition is well established the infant is so "floppy" that he will slip through the hands if an attempt is made to lift him.

Red or Pink Hands and Feet.—The extremities usually present a pink or red puffy appearance, especially on the hands and feet. In addition they feel "cold and clammy", or "like a frog", as the mothers often describe them. These are the so-called "raw beef hands and feet". The tip of the nose and the ears and the cheeks are also pink and cold. Later the extremities may desquamate freely, this adding to the irritability and general wretchedness.

Rash.—The rash is soon generalized in distribution, varies in intensity at first and then becomes persistent. It is often maculo-papular, "measly" or "scarlatinal" in character and is primarily sudaminal in nature. It is frequently followed by desquamation over the body, and the extremities in particular. The buttocks on occasions are deeply excoriated. With the lowered resistance of the infant and the constant scratching and "soggy" state of the skin from the free skin action, secondary infection is commonly seen and may present as impetigo, or as pustular or furuncular lesions. In extreme degrees gangrene may supervene and leave scarring and deformity of fingers and toes should the baby survive. In a few instances a true *cancrum oris* has been noted.

Sweating.—Sweating occurs almost always and is one of the most troublesome manifestations. It may be localized to the scalp or a limb; more often it is generalized and profuse, and in some babies sweat can be seen literally oozing from the body surface on examination. With this very free skin action there is often a characteristic "mousy" odour about these infants. Long-continued and profuse sweating can dehydrate these children severely and is often of serious prognostic significance.

Tachycardia.—The very hurried heart rate is certainly the most constant and persistent of all the clinical manifestations of this disease. It is present early in the illness and persists throughout the entire active phase without any intermission even during the short periods when the baby does have a few hours of sleep. This is very obvious on inspection of a chart upon which the sleeping pulse rate is recorded in conjunction with usual figures throughout the day. The actual rate varies from 160 to 180 or even over 200 per minute. The fact that these high rates are sustained for some considerable time is always a cause for concern, and doubtless throws a severe strain on the infant myocardium; this probably explains the very acute peripheral circulatory failure which occurs only too often in these patients. On account of the possibility of this fatal complication one must always be very guarded as to prognosis with these babies for the first eight to ten weeks of the illness. A nurse may have fed one of these infants and reported that his condition is reasonably satisfactory, and in perhaps half an hour finds him dead in the cot. Once the tachycardia begins to subside it can be taken as one of the most definite signs of commencing improvement in the clinical picture.

Hypertension.—Considerable increase in the blood pressure readings is almost equally characteristic of pink disease. The figures may be in the region of 140 millimetres of mercury (systolic) and 90 millimetres (diastolic) to 170 millimetres of mercury (sytolic) and 110 millimetres (diastolic). These figures are very high for infants of this age group, in whom the pressures would normally be in the vicinity of 80 to 90 millimetres of mercury (systolic) and 55 to 65 millimetres (diastolic). Improvement in the clinical picture is generally accompanied by a gradual fall of blood pressure, which proceeds more or less in parallel with the gradual subsidence of the tachycardia. The hypertension appears a little anomalous when it is seen associated with the extreme degree of apathy and loss of general tone in a baby who can be very aptly described as "floppy". Nevertheless, there is no doubt that the combination of tachycardia and hypertension over a number of weeks predisposes to the tragically sudden deaths which occur in some of these cases.

Insomnia.—Insomnia is a most obstinate and distressing accompaniment, and is a very characteristic feature of the disease, especially in the early stages of the illness. It is most resistant to treatment with many and various sedatives, and eventually leads to one or both parents becoming almost distracted as a result of loss of sleep themselves.

Stomatitis.—Stomatitis is a frequent complication in the active stages of the disease and can lead to much discomfort and inability to take nourishment; in this way it contributes to the rapid weight loss. In some infants with lowered resistance the constant grinding of teeth has led to a spread of infection involving the mandible.

Other Features.—Often at the onset of the illness gastro-intestinal disturbance occurs with vomiting, diarrhœa and sometimes colicky abdominal pain. Pallor is evident in many of these babies, especially after some weeks of the disease, and may be the indication of actual anæmia found when a blood investigation is carried out. Another point of interest lies in the fact that many mothers state that the illness began some little time after some previous infection following which the baby has never completely recovered.

The following clinical history, as related by the mother, is characteristic of pink disease. The patient is a male infant, aged twelve months. His illness commenced eight weeks ago with constantly "running eyes" and a generalized red and irritable rash. Four weeks ago he became intensely cross and not interested in feedings, and hardly slept at all at night. The palms and soles and the legs are particularly affected by the rash, and the baby is very resentful of light, frowning and burying his face on the mother's shoulder. He has been sweating profusely about the head for several weeks and has lost a considerable amount of weight in this time. Before the onset of the illness he was walking, but now he is unable to do so and just "flops" if stood upon his feet.

In individual cases there are numerous variants from such a clinical story as that just quoted, and it is worthy of note that all the characteristic manifestations are not evident in every child suffering from pink disease.

One has observed on a few occasions a rather sudden onset with a watery coryza for several days which, however, does not become purulent like the ordinary bacterial infection. With these infants there has also been the interesting fact that the mother had also suffered from a similar type of coryza about ten to fourteen days previously.

Causation.

Post-mortem findings do not give any significant help in the problem of elucidating the cause of pink disease.

Approximately one-half of the deaths are due to sudden circulatory failure, often associated with a severe respiratory tract infection, such as bronchitis, bronchopneumonia, or bronchiectasis, but approximately one-third of these circulatory deaths are due to myocardial failure alone.

In about one-third of all the deaths involvement of the gastro-intestinal tract is the outstanding feature, the principal lesions being enlarged and œdematous mesenteric glands resulting from acute gastro-enteric or entero-colitic lesions and less commonly actual superficial ulceration over engorged lymphatic nodules. The remaining small proportion of deaths is due to other complications like mastoiditis, severe skin affections and pyelonephritis.

Over the years numerous possible causative factors have been suggested, scrutinized carefully, and in turn discarded as the investigations have failed to confirm the original suspicions.

These include food, mineral or vitamin deficiency, bacterial infection, endocrine disorders and sodium or chloride depletion.

Up to the present time none of these suggestions has stood the test of careful inquiry or laboratory investigation.

From clinical investigation and inquiry alone there still appears to be considerable evidence in favour of a virus infection. Points in this respect are the history suggestive of case-to-case contact, waves of incidence showing "periods" of activity, and in addition distribution in certain areas during different ones of these periods. In addition there is evidence of family susceptibility to the condition, three and even four children of the one family being recorded as suffering from pink disease during the appropriate age. Finally, there is frequently evidence of family predisposition to the virus group of diseases—namely, measles, German measles, varicella, mumps, herpes—occurring in association with pink disease.

The most recent theory is the idea that the syndrome is a manifestation of sensitivity in certain infants to mercurial poisoning as a result of administration of teething powders containing calomel, or the application of mercurial ointments or lotions. This, like most of the previous theories, appears on the first presentation to be reasonably well supported by the data produced, but it is felt that considerably more evidence must be accumulated before this claim can be substantiated. In this respect I can recall many cases of infants suffering from pink disease, some of the most severe examples being included, in which careful questioning reveals that the infant has never had teething powders, nor has any mercurial application or mixture been used.

Diagnosis.

The differential diagnosis is surrounded with numerous problems. In the earliest phase it is frankly impossible to forecast that a particular baby is developing the trouble, but once it is well established it is almost impossible to mistake the clinical picture of abject misery for anything else. It is during the intervening period between these two extremes that most difficulty arises.

Vitamin deficiencies, poliomyelitis, "post-concussion" state, pyobacilluria, otitis, early meningeal infection, acute nephritis, the hyperkinetic state, and even cerebral tumour can all simulate pink disease very closely at certain stages of the illnesses and may be extremely difficult to differentiate without very careful history-taking, physical examination and observation of the infant, and assistance from colleagues in the pathology laboratory.

Prognosis.

Once the diagnosis is definite, the parents should be warned of the particularly long and tedious course of the illness—this applies both to the patient and to themselves—as it may amount to twelve months or more in obstinate cases. The immediate prognosis must of necessity be guarded in considering the first six to eight weeks of the disease, on account of the possible risk of sudden circulatory failure. The ultimate outlook, although quite good as regards the great majority of sufferers, is not always so satisfactory, and the more one sees of these babies and follows up their late results the more one realizes that quite an appreciable proportion are left with very definite and even severe sequelæ. These may include failure to thrive, personality changes and mental retardation even to the degree of necessitating training in special institutions, a Parkinsonian syndrome, trophic changes in the extremities and disturbance of sphincter control involving both bowel and bladder.

Bronchiectasis occurs in an appreciable number of children who have suffered the complication of severe bronchopneumonia. A small number of children has been seen in whom there was gross impairment of the sense of smell.

The occurrence of these sequelæ serves as a real reminder that one must not be over-optimistic in forecasting the final result.

Management.

Treatment and management provide a very difficult problem for the clinician. In the first place, because no definite cause is at present known, there is, of course, no specific line of therapy which will offer an immediate and satisfactory response.

The most important aspects of management will include nourishment, rest and avoidance of intercurrent infections.

Milk foods in various modifications are the most valuable form of nourishment, and are sometimes best administered as small feedings at frequent intervals, rather than as larger meals at set times. By adopting this procedure it is possible to guide a baby through this illness with little or no loss in weight or exceptionally with a slight gain.

Rest is essential for the child, and numerous sedatives have been tried, but many have not brought about the desired effect. Some even seem to act "in reverse" and stimulate the infant rather than quieten him.

Avoidance of intercurrent infection is essential, and this is one of the principal reasons why it is considered wiser to keep pink disease babies out of hospital wards. However, occasions arise when the mother simply cannot carry on at home, or the baby has developed some serious complication; it is then necessary to have the baby cared for under efficient nursing conditions, and herein lies the need for scrupulous care against the risk of intercurrent infection, particularly respiratory tract, gastro-intestinal and skin troubles.

ROBERT SOUTHBY,
Melbourne.

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British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on April 30, 1953. at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. A. J. MURRAY, the President, in the chair.

Disseminated Lupus Erythematosus.

DR. HELEN M. TAYLOR read a paper entitled "Systemic Lupus Erythematosus" (see page 403).

DR. R. B. PERKINS read a paper entitled "Disseminated Lupus Erythematosus" (see page 401).

DR. V. J. MCGOVERN discussed the pathology of systemic *lupus erythematosus*. He said that the lesions fell into two main groups, fibrinoid degeneration of collagen and fibrinoid changes in vessels. The skin lesions usually showed no fibrinoid change, but they were in other respects characteristic, although acute lesions of the localized discoid type were indistinguishable from the lesions of the acute disseminated systemic variety. Fibrinoid degeneration of collagen might be found in the interstitial tissues of the myocardium, and when they healed they caused focal fibrosis. That fibrinoid change in the collagen was the basis also of the verrucous endocarditis, which resembled that seen in rheumatic fever, but which often involved the mitral and tricuspid valves, but might affect the aortic valve alone. Similar alteration of collagen was responsible for the damage to serous surfaces such as synovial membrane. The vascular lesions were sometimes widely distributed, but at other times they were found only in a few organs. They consisted in fibrinoid thickening beneath the endothelium of capillaries. The thickening was often focal, and a projection of that material into the lumen in the form of a lump was fairly characteristic. Organs so involved usually contained some signs of inflammation with cellular infiltration. Hepatitis of severe degree had been seen in a recent case. The characteristic renal changes were due to fibrinoid thickening of the glomerular capillaries, and globoid masses of that material might also be seen. In the kidney the lesions were focal. Often one portion of the glomerulus showed that change, while the remainder had an appearance resembling glomerulonephritis of the exudative type. The glomerular changes were present in 60% of cases, but in only about 40% was severe renal insufficiency a feature. In severe cases, vessels, including the glomerular tufts, might proceed to necrosis.

Dr. McGovern went on to say that a characteristic autopsy finding, present in 95% of cases, was lamination of collagen around arterioles in the Malpighian bodies of the spleen. The exact nature of that change was unknown. Diagnosis at autopsy depended upon finding some or all of the changes mentioned. The renal changes occurred occasionally in dermatomyositis and scleroderma; but that was so rare that ordinarily those two disorders did not enter the differential diagnosis. Furthermore, the pattern of disease in them was different. Diagnosis by biopsy was rendered fairly certain by the finding of the *lupus erythematosus* cell and by demonstration of the characteristic skin changes. In the rare cases of diffuse scleroderma with an erythematous and œdematous skin rash the characteristic collagen change of that disorder was still found, and in the heart, too, the dense fibrosis of scleroderma was easily distinguished from the fibrinoid collagen degeneration of *lupus erythematosus*. Each disease exhibited collagen change, but of different types. Dr. McGovern said that dermatomyositis did not resemble *lupus erythematosus* microscopically. Although the changes in the skin, muscles and nerves were individually non-specific in that malady, they became characteristic in the over-all pattern. The histological appearances in systemic *lupus erythematosus* did no more than hint at the grave disturbance of metabolism which must be present.

DR. ADRIAN JOHNSON said that throughout the world there was a great deal of interest in *lupus erythematosus*, for three reasons. The first was the introduction of mepacrine in the treatment of the chronic discoid type. The second was the control of the acute form of the disease by cortisone. The third was the increase in the incidence of the disease. Dr. Johnson thought that the increase in incidence must be real and not apparent. With regard to mepacrine, the general consensus of opinion in such places as Leeds was that if chronic discoid *lupus erythematosus* was treated by that drug, one-third of the patients were cured, one-third had an improvement and then a recurrence, and one-third showed no change whatever. Another point about treatment with mepacrine was that occasionally it precipitated the patient into an attack of acute *lupus erythematosus*; that had been seen to occur in two cases at the Mayo Clinic. The general consensus of opinion, expressed at a symposium on *lupus erythematosus*, was that pregnancy did not affect the course of chronic discoid *lupus erythematosus*, and the presence of acute *lupus erythematosus* was not an indication for termination of pregnancy. With regard to the use of cortisone in acute *lupus erythematosus*, Dr. Johnson said that the crisis could be controlled by it, and the general opinion seemed to be that cortisone and its allies would not cure the disease, but were great aids in helping the patients to ride out the storm from which they might be going to recover. Referring to mepacrine and its effect, Dr. Johnson said that possibly it had the same effect as the old ultraviolet barrier creams. Some other light sensitization eruptions, such as Hutchinson's prurigo, seemed to be relieved by it also. Finally Dr. Johnson said that he would like to hear further discussion on the significance of *lupus erythematosus* cells, although he thought that Dr. McGovern had expressed the consensus of world opinion; but that opinion was certainly not held by some other pathologists in Sydney.

DR. F. GOLDSCHLAG said that he was essentially in accord with the opinions expressed by Dr. Taylor and Dr. Perkins about the various aspects of the mysterious disease under discussion, but he had several points to emphasize. The first was the fact that the name of the disease was unfortunate. The word *lupus* denoted tuberculosis, and *lupus erythematosus* had no connexion with tuberculosis; most investigators were agreed on that point. Clinically and histologically, what was important was that one could see all the transition from chronic to acute forms of the disease. There was no single pathological change which allowed a definite diagnosis to be made. Even the existence of *lupus erythematosus* cells was not definitely proved, and the signs and symptoms relating to the cardio-vascular system were not characteristic and not constant. The same histological changes might be found in a specimen from any chronic discoid lesion, as in the acute types of the disease. What Dr. Taylor had said about the predilection of the acute type for women was true, but that did not hold for the chronic form. The symptoms were very variable in the acute form. However, Dr. Goldschlag said that he emphatically refused to admit that acute *lupus erythematosus* could exist without skin manifestations. Skin manifestations would occur at some time during the course of the illness; they might appear and disappear, but they would always be present at some time. Referring to the differential diagnosis, Dr. Goldschlag said that erysipelas had to be considered; Kaposi had described his first case as *erysipelas perstans faciei*. Other conditions to be considered were typhus, pemphigus, *erythema multiforme* and *periarteritis nodosa*. With regard to treatment, Dr. Goldschlag said that the clinician had a great responsibility. He must protect the patient, not allow him to be exposed to sunlight, institute bed rest and avoid all active treatment; no surgical treatment at all should be undertaken. Sometimes very severe abdominal pain was present, simulating a surgical condition in the abdomen. Any surgical intervention in an acute case would end in disaster, even the extraction of a septic tooth. Dr. Goldschlag said that he was not impressed with cortisone in one case of lupus seen also by Dr. F. C. Florance. However, he would not hesitate to give cortisone in acute cases. Sulphonamide drugs should not be given in an acute case. The best treatment was to be as conservative as possible.

DR. R. F. A. BECKE said that he wished to draw attention to an interesting point in history. The disease had first been described under the name of *lupus erythematosus* by Cazenave in 1833. On the clinical side, Dubois, writing in a recent symposium, said that typical butterfly lesions appeared on the face in only one-half of the cases of systemic *lupus erythematosus*; various non-specific rashes also occurred. Of one recent series of 18 cases, in only 11 was there a rash. It had been estimated that one-third of all cases of systemic *lupus erythematosus* at the Mayo Clinic between 1938 and 1947 commenced as the discoid type of the disease; that seemed to bear out the fact that all types were phases of the one disease and that all grades could be seen. Montgomery had said the same in his text-book. Many patients had spontaneous remissions. The incidence of spontaneous remissions was frequently reduced by the administration of ACTH and cortisone. An interesting case at the Royal North Shore Hospital of Sydney was one of subacute disseminated *lupus erythematosus*. The condition was not in the acute category, but the patient had a mild febrile reaction and was treated with ACTH and cortisone. Three or four months prior to the meeting the treatment was stopped. The patient had had other types of treatment since then and had yet to relapse. Dr. Becke went on to say that massive doses of hormones were given in the initial stages,

up to 100 or 200 milligrammes an hour for the first twenty-four hours until the condition had settled down; then the dosage was greatly reduced, and finally the patient had a maintenance dose. In Sydney large doses of vitamin *C* were given, up to one gramme daily, replacement therapy was employed, and testosterone was given in doses up to 500 milligrammes per day. Referring to the L.E. cell, Dr. Becke said that some people regarded it as an artefact. If it was so, it would seem to be one that was fairly specific for that disease, as it occurred in almost 100% of cases of the disease in which fever was present.

DR. E. J. C. MOLESWORTH said that he wanted to hear something on the completely divergent views of the physicians and dermatologists. He had heard it said recently by physicians that the chronic discoid type did not lead to the disseminated disease. He had also heard it said recently by a leading Sydney pathologist that the L.E. cell was "the bunk". As Dr. Taylor had pointed out, the dermatologists had been treating these patients longer than the physicians, and they had seen the end result of conservative treatment. Referring to pregnancy in *lupus erythematosus*, Dr. Molesworth said that it might or might not be true that the disease would go into remission with the daily administration of 500 milligrammes of ACTH or cortisone. As the disease was likely to be quickly fatal to the fœtus and the mother, as he had seen, the question of treatment with hormones had to be considered. Dr. Molesworth challenged the meeting to make a statement on whether the disease did exist without skin lesions and whether the L.E. cell was 'the bunk" or not, and he asked the President whether the use of ACTH or cortisone in large doses in the treatment of a pregnant woman was defensible. He apologized for being provocative, but said that he hoped that by such an attitude some exchange of ideas might be achieved.

DR. JAMES ISBISTER said that he had been interested in the statement made by Dr. Perkins, which had been refuted by other speakers, that there was a continuous gradation from the small localized skin lesion to the systemic form of the disease. Also there was the question whether the disease did or did not occur without skin manifestations. He was not in a position to give the answer; but he thought that the reason why Dr. Molesworth said that physicians were new to the disease was that patients with chronic skin disease did not first consult a physician. The physician saw a patient complaining of symptoms like fever, arthritis or malaise. Dr. Isbister went on to say that whether the disease was more common at the present time than previously it was impossible to say; physicians had always admitted that they saw many cases to which they could put no diagnostic label. That had occurred in the past, and no doubt some were forms of *lupus erythematosus* with few or no skin manifestations. Only recently had they become conscious of the occurrence of these conditions. The two cases he had encountered in the last year or so in the general medical wards had had the diagnosis of rheumatoid arthritis, pyrexia of unknown origin *et cetera*; one patient had a skin rash on one extremity which lasted for two days; the other had no skin rash but œdema of the face. Dr. Isbister felt that the dermatologists had an unfair advantage in having the disease more or less written for them on the skin.

DR. K. S. HARRISON said that he thought the descriptions given by the two speakers had been very clear, but that those present might go away with too precise a picture of patients with nicely graded rashes. Physicians were confronted with problems which often were not so clear cut as that. They saw patients with a rash, fever, albuminuria, and some red cells in the urine, and the dermatologist might label the eruption as "toxic". Dr. Harrison said that several cases of Henoch-Schönlein purpura had been encountered at the Royal Prince Alfred Hospital over the last few years and that condition might cause confusion in diagnosis. In those cases the blood vessels involved appeared to be intermediate in size between those affected in systemic *lupus erythematosus* and in *polyarteritis nodosa*. The three disorders might be very difficult to distinguish at times, both clinically and pathologically, though Dr. McGovern thought that the histological appearances were usually characteristic. Dr. Harrison did not know what part the collagen played in those disorders, as it had always seemed a mysterious substance to him. Some recent papers had shown the appearance of collagen under the electron microscope, so perhaps future studies of the diseases by that means might clarify the picture.

DR. S. MARSHALL referred to the differential diagnosis. He said they had spoken about it, but emphasized one point: in *lupus erythematosus*, whether localized or diffuse, there was sensitivity to light. That sensitivity was not present in the other diseases mentioned. If a patient suffering from *lupus erythematosus* was exposed to sunlight the action would soon be regretted. The pain was generally widespread and muscular too, and that pain often lasted much longer than the arthritic pain. Dr. Marshall said that he had found cortisone effective, but sometimes remissions were only partial, and if the dose was reduced to 50 milligrammes a day the lesions began to appear again. Dr. Marshall thought that in most cases the minimum dose was about 75 milligrammes a day. He felt, as most dermatologists, that *lupus erythematosus*, whether discoid or systemic, was the same disease. To talk of a clinical diagnosis of *lupus erythematosus* without skin lesions was rather difficult. Dr. Marshall did not see how the diagnosis could be made without them. As Dr. McGovern had said, even the post-mortem changes were not definite. Now there was the L.E. cell, which would aid the diagnosis without skin lesions; his patients had it too. According to Hargraves, examinations of other blood and serum did not reveal the L.E. cell. Another point about the cell was that if the serum of a patient with *lupus erythematosus* was taken and used to treat the blood of a normal person, L.E. cells would be produced in that blood.

Dr. Perkins, in reply, said that Dr. Becke had given him the impression that he thought that Cazenave was the first person to describe *lupus erythematosus* under the title of centrifugal erythema. Dr. Perkins understood that Biett was the first person to describe the disease, under the title of *erythème centrifuge*, and Cazenave followed about thirteen years later. Dr. Perkins said that Dr. Marshall had given him the impression that he thought all patients suffering from *lupus erythematosus* were sensitive to light; actually at the Mayo Clinic, of patients with the third, fourth and fifth clinical types of the disease which he had described in his paper, 56%, 40% and 22% respectively were sensitive to light.

Dr. Taylor, in reply, said that in her opinion the L.E. cell was not "the bunk". Referring to the occurrence of *lupus erythematosus* in pregnancy, she said that a pregnant woman with the disease in an acute form was very ill, and her medical attendant was in a very difficult position. As Dr. Goldschlag had pointed out, operative procedures even of the most minor nature must be avoided. One might try conservative treatment and see what mepacrine would do.

Dr. McGovern said that at the Royal Prince Alfred Hospital one was reluctant to diagnose the presence of *lupus erythematosus* cells unless undoubted examples were seen. In one of the cases quoted by Dr. Perkins two cells were seen in a film which might ordinarily pass for *lupus erythematosus* cells, but they were not typical examples. Referring to discoid lesions, Dr. McGovern said that in any chronic dermatological inflammation histological examination usually revealed hyperplasia of the epidermis and hyperkeratosis. The early stages of the discoid lesions did appear identical with the acute lesions, and if one subtracted the hyperkeratosis and patchy acanthosis of the epidermis from the appearances in a chronic lesion and added a little œdema to the dermis, the result would be acute *lupus erythematosus*. Referring to the possibility of the occurrence of *lupus erythematosus* without a rash, Dr. McGovern said that recently two patients had come to autopsy at Royal Prince Alfred Hospital who had had no characteristic rash, although one had had a purpuric rash. Each patient had the characteristic lesions, including the renal lesions, which occurred in only 60% of cases, but when they did occur they were regarded as characteristic. One patient had verrucous endocarditis and characteristic vascular and renal lesions. Dr. McGovern said that the latter patient had been thought to be suffering from a very unusual form of rheumatic fever, but the pathological changes were those of *lupus erythematosus*. There were patterns in disease, and even if a portion of the pattern was omitted—namely, the rash—the over-all pattern should still be recognizable.

Dr. Murray, from the chair, said that Dr. Goldschlag had aptly referred to *lupus erythematosus* as a mysterious disease. Those present had learnt enough to know that real steps were being taken to solve the mystery. Dr. Taylor had commented on the interesting observation that there was a variation in the patient's reaction to testosterone according to whether the disease was *lupus erythematosus* or not. Possibly a clue to the solution of the mystery lay therein, and no doubt it was being followed up.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal North Shore Hospital of Sydney, Crow's Nest, New South Wales, on April 23, 1953. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical

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staffs of the hospital. Part of this report appeared in the issues of July 25 and August 1 and 15, 1953.

Pulmonary Tuberculosis.

DR. BRUCE WHITE showed a woman, aged twenty-seven years, who had been admitted to hospital on February 14, 1953, with a past history of cough and sputum for twelve years. Pulmonary tuberculosis had been diagnosed in 1942 by X-ray examination. She had had hæmoptysis in 1945 and 1951. She was admitted to hospital for surgical treatment, having had much blood-staining of the sputum since 1952 and X-ray appearances suggestive of cavitation in the upper lobe of the right lung. That lobe was resected by Dr. Ian Monk on March 4. The specimen from the operation was found to contain a cavity near the apex, two centimetres in diameter, and several smaller areas of consolidation. While in hospital the patient received streptomycin and PAS. Her convalescence was uneventful and on April 7 she was discharged to her home for bed rest and treatment with streptomycin and PAS. Post-operative X-ray examination showed the lung to have expanded well, and there was no evidence of fluid or disease.

Dr. White also showed a woman, aged twenty-nine years, who in May, 1951, had suffered from an acute respiratory infection associated with tiredness, listlessness and fever. Laryngitis followed with hoarseness of voice. X-ray examination at that time showed infiltration in the upper zone of the left lung, the appearances being consistent with a tuberculous infection. A number of specimens of her sputum were examined, the results all being negative for acid-fast bacilli, with the exception of one in which acid-fast bacilli were found. In October, 1951, she suffered acute pain in the left hemithorax with severe dyspnœa. Her lung was said to have collapsed. The patient was transferred from Inverell to Tamworth Base Hospital, where bronchoscopic examination revealed granulation tissue obstructing the left main bronchus. That was removed and the lung reexpanded. Further bronchoscopic examination was made in November for the same reason. In view of the radiological findings, *plus* the presence of acid-fast bacilli in one specimen of sputum, it was felt that the patient's condition was due to a tuberculous infection of the left main bronchus. She was admitted to the Royal North Shore Hospital of Sydney and given streptomycin and PAS with improvement. In June, 1952, she again suffered severe pain on the left side of her chest and said that she felt her chest "flop". She was admitted to hospital, and after further investigation left pneumonectomy was performed because it was felt that irreparable damage had been done to the left lung following stenosis of the left main bronchus. After operation she was transferred to Princess Juliana Hospital, where her general condition improved, and she was discharged from hospital in March, 1953, to return to her own home for further convalescence. At that stage her general condition was excellent; she had no cough or suutum, and there was no clinical, radiological or pathological evidence of disease in the right lung.

DR. C. G. BAYLISS showed a man, aged twenty-four years, who had reported for examination in March, 1952, with a history of feeling rather tired for six months and losing three stone in weight, some of which he had regained. He had no cough and no family history of tuberculosis. He was a tall man, weighing eleven stone three pounds, and not obviously ill. The only abnormality found on chest examination was in the form of broncho-vesicular breath sounds in the apical region posteriorly on the right side. The result of a Mantoux test was postive. Culture of fasting gastric contents was carried out, but no tubercle bacilli were recovered. The X-ray appearances of the chest suggested tuberculous infiltration affecting the apical and subapical region of the right lung. A tomogram suggested the presence of cavitation. A diagnosis of tuberculosis was made, and the patient was admitted in May, 1952, to Princess Juliana Hospital, where he was given the usual sanatorium treatment, but no specific therapy. His general condition steadily improved, and serial X-ray films of the chest indicated clearing of the disease up to the point when it was felt that the limit of immediate improvement had been reached. The more active disease appeared to have resolved, but a moderate amount of infiltration remained, with low-grade activity. It was thought that over a lengthy period that condition might virtually become stable; but in view of the patient's good general condition and apparently good native resistance, resection of the upper lobe was considered to offer a quicker and more certain prospect for the arrest of the disease. Accordingly, the lobe was resected by Dr. Ian Monk in November, 1952. Examination of the resected lobe showed large caseous areas in the posterior and apical segments, fusing in some parts up to a mass three centimetres in diameter. One nearby bronchus was dilated, but the anterior part of the lung appeared to be normal. Microscopic examination of a section from the edge of the caseous area showed chronic tuberculosis with considerable fibrosis. Tubercle bacilli were present. Convalescence was uneventful, and Dr. Bayliss considered that the course of the patient's disease to date gave every hope that stabilization and arrest of the disease was being achieved.

DR. A. G. MCMANIS showed a man, aged forty-seven years, who in February, 1952, had developed pneumonia which failed to respond to treatment. A persistent cough with sputum and hæmoptysis followed. X-ray examination of the chest showed consolidation in the anterior segment of the upper and middle lobes of the right lung. Direct smear examination disclosed the presence of acid-fast bacilli in the sputum. In view of the segmental nature of the lesions, bronchoscopic examination was performed to see if there was any endobronchial disease, but none was found. The patient was put to bed and given streptomycin and PAS. He was a diabetic of many years' standing who had been treated by diet alone; but the diabetes could not now be controlled by diet, and insulin was prescribed. After a period of complete rest a tomogram confirmed the fact that the lesions were solid in type. Because of that, surgical treatment was thought desirable, and in September, 1952, the upper and middle lobes of the right lung were resected. Post-operative progress was satisfactory. A possible spread of disease in the lower part of the left lung was suspected, but the opacity completely cleared. Dr. McManis said that since operation the patient had had no sputum, and repeated smear and cultural examination of gastric contents had given negative results. The patient was discharged from hospital in March, 1953, in a very satisfactory general condition. His blood sedimentation rate, which had been 14 millimetres in one hour at the time of admission to hospital, had fallen to six millimetres in one hour.

Carcinoma of the Breast with Spinal Metastases.

DR. A. R. HAMILTON presented a woman, aged fifty-four years, who had been admitted to hospital in March, 1952, with paraplegia. Three months previously she had experienced backache in the lower dorsal region, followed two months later by severe girdle pain passing round the abdomen midway between the xiphisternum and umbilicus. Four days before her admission to hospital she developed weakness of the legs, and on the following day her legs were completely paralysed. Flexor spasms were experienced in both lower limbs, and she had retention of urine and fæces. Examination of the patient revealed a transverse lesion of the spinal cord in the region of the ninth thoracic segment. Complete sensory loss was found below that level, with increased knee and ankle jerks and bilateral Babinski signs. No tenderness or deformity of her spine was present. A fixed tumour in the right breast was considered to be a scirrhous carcinoma. X-ray examination of her spine showed collapse of the ninth dorsal vertebra, highly suggestive of metastatic malignant disease. The patient was nursed with her back hyperextended, and 50 milligrammes of testosterone were given three times a week. Sensory loss became greatly diminished, movement began to return to the legs, and sphincter control was regained. After consultation with the honorary radiotherapist, the patient was transferred to the Royal Prince Alfred Hospital for deep X-ray treatment on April 21, 1952. Returning on May 8 for reeducation and physiotherapy, she then stated that all her girdle pains had disappeared and she felt much better. Graduated walking exercises were commenced with the aid of a spinal brace. The administration of testosterone propionate was continued. The patient's ability to walk unaided improved greatly, and she was discharged to a convalescent home in June, 1952. Dr. Hamilton said that the patient was still able to walk with the aid of a spinal brace, which was soon to be discarded. He thanked Dr. I. A. Brodziak for permission to present the patient.

Carcinoma of the Cervix and Pregnancy.

DR. A. J. MURRAY showed a married woman, aged twenty-eight years, who had been first interviewed two weeks prior to her admission to hospital, when she complained of amenorrhœa for three months, followed by slight vaginal bleeding for two weeks. Examination of the patient revealed a fungating fleshy tumour arising from the uterine cervix. Examination of a biopsy specimen revealed squamous carcinoma with only a moderate degree of anaplasia, but fairly numerous mitoses. When the patient was admitted to hospital, the cervical tumour was found to have increased in size, and an abdominal mass arising from the pelvis was also discovered and thought to be due to a sixteen-weeks

pregnancy. Total hysterectomy was carried out, with removal of the upper third of the vagina, bilateral salpingo-oophorectomy, and bilateral excision of the external and internal iliac glands. The left internal iliac group of glands was indurated and adherent to the side wall of the pelvis, and the uterus was found to contain a sixteen-weeks fœtus. Convalescence was complicated by persistent pyrexia, probably due to pelvic cellulitis; it responded dramatically to penicillin therapy. The pathology report stated that the cervical mass was a well-differentiated squamous carcinoma, a deposit of which was present in the left internal iliac lymph node. The other lymph nodes and the vaginal walls contained no malignant tissue. The patient was now to have a course of deep X-ray therapy.

Prolapsus Uteri.

Dr. Murray, with DR. W. G. JASPER, presented a group of patients to demonstrate the possibility of vaginal hysterectomy, both in women who were leading an active sexual existence, and in those who were long past that stage. He said that age was no bar to the operation, as one of the patients was aged eighty-two years and another aged seventy-two years. Unfortunately, many such women were condemned to a "pessary existence", and many practitioners did not realize how well elderly women tolerated the operation and how much comfort it would give them. It was pointed out that vaginal hysterectomy was indicated in all cases of third degree prolapse, and in lesser degrees of prolapse where there was, in addition, some indication for removing the uterus for non-malignant disease.

Marchetti Operation for Stress Incontinence.

DR. STUART B. STUDDY showed a married woman, aged forty years, who had suffered from incontinence of urine for twelve months. It had begun as stress incontinence, but had become worse and was now continuous and was aggravated by stress. The patient had three children, the youngest aged fifteen years. She had undergone Fothergill's operation eleven years previously, and a vaginal plastic operation for cure of stress incontinence four years previously. Examination of the patient revealed an excellent anatomical result from the previous vaginal plastic operation. No urethrocele or cystocele was found. The uterus was anterior in position and normal; the fornices were clear. Marchetti's operation of vesico-urethral suspension was carried out. On the patient's discharge from hospital, no evidence of stress incontinence was present; and when she was examined four and a half months later, she had an excellent result with good urinary control. Dr. Studdy said that the Marchetti operation, devised by Marshall and Marchetti, had been employed for stress incontinence for the first time in 1944. He described its main features. The bladder was filled by inflating a balloon inserted on the end of a catheter, and the patient was placed in the Trendelenburg position. A suprapubic incision was made to expose the space of Retzius widely. The bladder and urethra were separated from the posterior surface of the pubis and rectus muscles down to near the external urethral meatus. An assistant's finger in the vagina aided palpation of the catheter and balloon, which corresponded to the urethra and vesical neck respectively. Three sutures of Number 1 chromicized gut were placed equidistant from each other on either side of the urethra. The suturing needle was inserted deeply into the upper wall of the vagina, adjacent to the urethra, and not into the lateral wall of the urethra. A similar suture was placed on either side of the vesical outlet in the angle between the balloon and the catheter. With a curved round-edged needle, the long ends of these sutures were placed securely through the periosteum of the pubis, especially into the cartilage of the symphysis whenever possible. If necessary, some of the sutures could be inserted into the rectus muscle. Additional sutures might be placed in the bladder musculature and rectus muscles to pull the bladder further anteriorly. A small rubber drain was placed in the space of Retzius in case of any urinary leakage. The drain was removed on the third day after operation and the catheter on the seventh day. Dr. Studdy said that the operation was not intended to replace the routine vaginal plastic operation for cure of stress incontinence, but was a further aid to cure in those cases in which the plastic operation did not bring relief.

Papilliferous Hydradenoma of the Vulva.

Dr. Studdy's second patient, a woman, aged thirty years, had been admitted to hospital for investigation of a vaginal discharge which had developed after childbirth four years previously. Examination of the patient revealed a chronically inflamed cervix and two small cysts on the left labium at the muco-cutaneous junction, one of which appeared to be filled with blood. The cysts were excised and submitted to pathological examination. The pathologist reported that the cysts were thin-walled and contained gelatinous material of a colour resembling putty. One cyst was multilocular and consisted of a pedunculated mass covered by stratified squamous epithelium. It was composed of a number of cysts lined by columnar or cuboid epithelium without cilia. Many papillary projections were present. The condition was a hydradenoma of the papilliferous type.

Carcinoma of the Vulva Treated by Radical Vulvectomy.

DR. EDMUND COLLINS showed a single woman, aged fifty-six years, who had reported to the hospital in January, 1953, complaining of pruritus and a small tender lump in the vulva for four months. She was found to have leucoplakia of the *labia minora*, with a small, hard, acutely tender lump in the fold between the left *labium majus* and left *labium minus*. Biopsy revealed the presence of a well-differentiated squamous carcinoma, and Stanley Way's radical vulvectomy operation was performed. No deposits of tumour were found in twelve lymph nodes examined. Convalescence was uneventful, and at the end of ten weeks the wound was healing well with formation of healthy granulation tissue.

Squamous Carcinoma of the Cervix Uteri.

DR. W. G. JASPER presented a married woman, aged sixty-three years, who had been admitted to hospital with a history of vaginal hæmorrhage for three months. Examination of the patient revealed that the *cervix uteri* was almost completely replaced by a large ulcer which had spread onto the vaginal fornices. A small papilliferous tumour was present in the vagina one centimetre from the edge of the ulcer. A biopsy report showed that the ulcerated area was squamous carcinoma. Radical hysterectomy was performed, with removal of all parametrial tissue, obturator, internal, external and common iliac and sacral lymph glands, and two and a half inches of vagina. As the patient was fat, access was sought, not through a mid-line incision, but through a V-shaped incision with the apex above the pubis, each *rectus abdominis* muscle being cut through transversely. When the abdomen was closed, no attempt was made to suture the muscle tissue itself, but the anterior rectus sheath was stitched with very fine interrupted "Nylon" sutures. The wound healed by first intention, and when the patient was examined six weeks after her discharge from hospital, no weakness of the abdominal wall was apparent. The pathologist considered that the papilliferous tumour was separate from that of the cervix, and if not already carcinomatous, was at least showing pre-malignant tendencies. In view of that report and the clinically unhealthy appearance of the vaginal mucosa, the remaining stump of vagina was removed from below two weeks after the previous operation.

Neonatal Anæmia.

DR. CLAIR ISBISTER presented a baby who had been suffering from neonatal anæmia. The baby had been born three weeks before the due date, but otherwise the confinement was normal. The mother had had no previous pregnancies or blood transfusions. Her blood group was O(IV) Rh-positive. She had suffered from mild toxæmia of pregnancy. At birth, the baby was very pale and a narrowing of the umbilical cord was noticed, described as "spasm". The baby was also lethargic, but no jaundice or petechial hæmorrhage was noted. The liver and spleen were not palpable, and there was no evidence of hæmorrhage or other sign to suggest hæmolytic disease. The baby's hæmoglobin value was 5·5 grammes *per centum* and his blood was Rh-positive. An urgent transfusion of 80 mils of A(II) Rh-negative blood was given. The baby's colour improved, but his condition remained poor. Administration of oxygen was maintained with five milligrammes of vitamin *K* every four hours. On the following day, the hæmoglobin value was 9·4 grammes *per centum*, and the baby was still pale. The pathologist reported a wide variation in size and shape of the red blood cells and large numbers of red blood cells of varying degrees of immaturity. The film was typical of hæmolytic anæmia. The result of a Coombs test was positive. A further 80 mils of O(IV) Rh-negative blood were given, and the baby's condition improved greatly, though he was still very lethargic and appeared ill. Two days later the hæmoglobin value had

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increased to 11·1 grammes *per centum*. Normoblasts were present in the blood, in a proportion of about 1·5%. The pathologist said that the film was one of hæmolytic anæmia, but transfusion or infection could cause that anæmia. Spherocytes were present. The result of a Coombs test was negative. Blood typing of the mother revealed that her blood was group O Rh-positive, CDe/CD/e anti c negative, and an immune antibody against A was present. Blood typing of the father revealed that his blood was group A CDe/cde anti c positive. The blood bank did not consider that the baby's condition was hæmolytic disease of the newborn. The baby was still not well. His colour was poor, his respiration rate and lethargy had increased, and as no cause had been found, infection was suspected. Terramycin, 25 milligrammes every six hours, was given for three days. At the end of that time, the hæmoglobin value was 14·7 grammes *per centum*, and the baby's condition was improved, but he still had to be tube-fed and was lethargic. Four days later, the hæmoglobin value was 17·9 grammes *per centum*, and the leucocytes showed signs of toxic variation. On February 6, when the baby was just one month old, the hæmoglobin value was 12·8 grammes *per centum*. Microscopic examination of the blood revealed moderate anisocytosis, moderate poikilocytosis and occasional spherocytes, but no nucleated red cells. By March 3 the baby's weight had increased to nine pounds fifteen ounces and he was being fully breast-fed. His hæmoglobin value was 9·4%, and blood examination showed polychromasia to the extent of 1% or 2%. The child was receiving a ferrous sulphate mixture. The mother had been in a mothercraft home and had persisted with breast feeding until the child became easier to feed. It now appeared that normal progress was being made. By the end of March the baby weighed 12 pounds 10 ounces, the hæmoglobin value was 12·8 grammes *per centum*, his condition was excellent, and progress was normal. Dr. Isbister said that the differential diagnosis of the cause of the anæmia lay between hæmorrhage from the umbilical cord during delivery, hæmolytic disease of the newborn and hæmolytic disease due to intrauterine infection.

DR. IAN BOOTH presented a baby who had been born on January 3, 1953, with a birth weight of six pounds five and a half ounces, being the third child of his mother. He became deeply jaundiced within forty-eight hours of birth and remained jaundiced to a lesser extent up to the time of his discharge from hospital at the age of five weeks. The spleen was palpable from the third day. The hæmoglobin value fell from 22·9 grammes *per centum* on the third day to 10·2 grammes *per centum* on the nineteenth day. Sixty mils of Rh-negative O(IV) blood were given intravenously on the twenty-first day. After the transfusion, the hæmoglobin value fell to 7·4 grammes *per centum*, and repeated readings on the following days showed values of 7·7 and 8·2 grammes *per centum*. On the twenty-ninth day, a further transfusion of 120 mils of Rh-negative A(II) blood was given, and his hæmoglobin value rose to 14·2 grammes *per centum*. The baby was discharged from hospital "well" at the end of five weeks, his weight then being seven pounds one ounce. When examined at the baby clinic at the age of six weeks, he was pale and had an icteric tinge, but he was bright and contented. The spleen was palpable two fingers' breadth below the costal margin. The liver was not palpable. During the next six weeks the baby continued to thrive and gained on an average 12 ounces per week. The spleen remained palpable; the hæmoglobin value fell gradually to 7·4 grammes *per centum*. No further transfusion was given. At the age of fourteen weeks, the baby had a hæmoglobin value of 8·6 grammes *per centum*, and the spleen was just palpable. Investigation of the family history revealed that the father, who was aged twenty-eight years, had undergone splenectomy at the age of thirteen years in England, after a ten years' history of splenomegaly without jaundice. Investigation revealed that at the time when the splenectomy was performed, the father had increased fragility of his erythrocytes. Examination of the father's blood on April 16, 1953, revealed increased fragility, hæmolysis commencing at a sodium chloride dilution of 0·52%. Examination of a stained blood film showed a tendency to spherocytosis. The baby's brother, aged six years, also had increased erythrocyte fragility, and examination of a blood film revealed the presence of spherocytes, much variation in size and staining of cells, and polychromasia in 7% of cells. Examination of the blood of the baby's sister, aged three years, revealed no abnormality. The baby's blood group was A(II) Rh-positive and the result of a Coombs test was positive. Examination of a stained blood film on January 9 revealed moderate anisocytosis and the presence of spherocytes. Examination of a further film on January 27 revealed considerable variation in the size of erythrocytes, with moderate anisocytosis, slight poikilocytosis, polychromasia to 2% and the presence of many spherocytes. A fragility test carried out on February 2 revealed that hæmolysis commenced at a dilution of 0·5% and was complete at a dilution of 0·32%. The comment was made that that very slight increase in fragility could be due to the presence of transfused cells. Subsequent blood examinations revealed persistent spherocytosis, anisocytosis, poikilocytosis and polychromasia to a variable degree. A fragility test on March 24 showed that hæmolysis commenced at a dilution of 0·5% and was complete at 0·35%. Dr. Booth said that there were three points of interest in the case: first, the Rh-negative mother with an Rh-positive baby; secondly, the possibility of transfusion hæmolysis; thirdly, the family history of splenomegaly. The diagnosis of the baby's condition was considered to be acholuric jaundice.

Congenital Abnormalities.

DR. F. N. STREET showed two children suffering from congenital abnormalities. The first was a mongol baby with a loud systolic heart murmur audible over the upper part of the sternum. The child had been born two weeks before the expected date of confinement, and had had a weight of five pounds and half an ounce and a length of eighteen and a half inches. The mother was a *multipara*, aged thirty-nine years, who had undergone lobectomy in 1942. Her blood group was O(IV) Rh-positive.

The other baby, who was the mother's first baby and had been born after a normal pregnancy, had an abnormality of the eyelids. The baby's father had the same abnormality.

DR. R. H. VINES showed two babies suffering from congenital amputation of the fingers. The first, a boy, aged three and a half months, had been born prematurely at thirty weeks' gestation. The mother had suffered from antepartum hæmorrhage during the pregnancy. The baby's birth weight was four pounds eleven ounces and his length 18 inches. His head circumference was thirteen and a half inches. He had multiple amputations and constriction rings of terminal phalanges. A band was found encircling the constriction rings. The pathologist reported that the band appeared to consist of solid fibrous tissue with a smooth surface, suggesting the possibility of epithelial surface, which, if present, would not have survived fixation. The other child, also a boy, aged three and a half months, had weighed seven pounds at birth and had measured 20 inches in length and 13 inches in head circumference. His mother had suffered from preeclampsia during pregnancy, and her blood group was B Rh-negative. The child had constriction rings of the fingers of the right hand and of the left wrist and amputation of the distal phalanx of the right middle fingers. He also had bilateral *talipes equino-varus* and a *café-au-lait* spot on the right shin. His progress had been good, and he had developed normally. His present weight was 17 pounds and his head circumference 16 inches. A further *café-au-lait* spot had appeared on the right side of the abdomen.

Pulmonary Lobe Collapse and Bronchiectasis.

DR. N. PERCY showed a baby, aged eighteen months, who, after a normal birth and neonatal period, had developed a slight cold and wheezing at the age of three months. From the age of six months he had suffered from repeated chest colds. At the age of ten months he had undergone circumcision under general anæsthesia, having at the time a cough and nasal discharge. From then on the cough became much worse. At the age of twelve months the child was admitted to the Royal North Shore Hospital of Sydney suffering from collapse of the middle lobe of the left lung, anæmia and salmonella enteritis. Bronchoscopic examination revealed the presence of pus in the right middle lobe bronchus. After four weeks the child was discharged from hospital, to be readmitted two months later suffering from pneumonia in the upper lobe of the left lung and the lower lobe of the right lung. He was now having breathing exercises, postural drainage, expectorants and nasal drops. Dr. Percy referred to a number of points of interest relating to the case. He pointed out the common association of nasal discharge and repeated chest infections and also the low emulsion intake of such children. The third point was the hazard of general anæsthesia, the child's habit of sleeping on the face predisposing to collapse of the right middle lung lobe. Mention also was made of the suggested causal association of aspiration pneumonia and bronchiectasis and the particular treatment difficulties at the patient's age.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

A QUESTIONNAIRE FROM ENGLAND.[1]

(Questions 1 to 9 and the answers to them were published in last week's issue.)

10. *What diseases prevail there?*

(A). There are no diseases incidental to this climate. The colony has always been remarkably healthy. Newcomers are frequently attacked with dysenteric affections and the hepatic functions are very irregularly performed especially in the summer. Fevers seldom occur. I do not believe there is any case on record of intermittent fever having originated in this colony previous to the year 1825. Since that period several cases have occurred during a long continued drought. The subjects of this disease are chiefly those who had resided in the vicinity of lagoons or marshes which had evaporated. Some of the cases, however, could not be traced to that cause. Intermittents have occasionally been imported into the colony and have not been found difficult to cure.

Dropsy in all its forms is more common here than any other country I have visited which may be accounted for by the dissipated lives most of the prison population have led prior to their conviction.

(B). Diseases of a purely febrile character are not very common among any order of the community. July, August and September are the months in which fevers are most prevalent and the simple continued is the usual form such as occasionally assume a remittent type, mostly affect children and elderly persons: among the middle aged they are not so common and intermittent as an endemic is entirely unknown.

The rapid and frequent changes of the winds and the great extent of forest land over which it blows may have some influence in preventing the recurrence of marsh fevers. To this may be added the generally good ventilation of the dwellings, the exercise which is taken by people in the open air and the frequent bathing that is resorted to by all classes. It may also be borne in mind that one great predisposing cause of disease arising from an inadequate quantity and inferior quality of food is not known here, while on the other hand the effects of intemperance and the dissolute lives of many are moderated by the salubrity of the climate.

Erysipelatous affections are common in summer and principally attack the young, but are never dangerous, as a mild purgative is generally sufficient to remove the complaint unless the patient by scratching ruptures the vesicles so as to cause ulceration which is sometimes troublesome.

In April, 1794, ulceration of the eyes was observed for the first time and was generally prevalent amongst all descriptions of people. It raged at first among children, but when it got into a house scarcely any person escaped it. They account for this complaint by the variable weather which then prevailed. Since that time the same disease has been very general at different periods. November, Decembr and January are the months in which it most prevails. The orphan institutions have been on several occasions distressingly affected with this complaint under different degrees of violence and duration. Cold water, vinegar, or brandy and water are the common domestic applications, and if used in time and with care and a little attention to the state of the bowels little more is required to effect a cure, but when the complaint is neglected or treated improperly the cure is difficult and protracted. Loss of vision has been the consequence in a few instances. Some of the children of the above Institutions were frequently observed to go to bed without the least appearance of ophthalmia and rise in the morning with the eyes completely closed up and the conjunctiva highly inflamed. From this circumstance a belief arises that mosquitoes or small flies carry the infection from one person to another. It is, however, only a common form of conjunctival inflammation and its treatment does not necessarily differ from the common forms of that affection. It is well known to the colonists by the name of "Blight": a different affection has existed amongst the troops, but is now declining.

In 1824 mumps were epidemic, the glandular swellings were almost invariably on both sides of the neck accompanied with unusual pain. Suppuration took place in a few instances succeeded by obstinate ulcers. In all other cases the disease was removed in the usual time. In July and August, 1820, epidemic catarrh prevailed throughout the colony: occasional cases of it had been appearing from the beginning of the year, but most families began at this time to suffer severely, there being hardly a house that had not cases of more or less danger. It proved chiefly fatal to infancy and old age: the symptoms of this complaint were common cold, cough, pains in the forehead, sneezing, soreness and spasm in the chest, copious discharge of mucus of various colours from consistencies from the lungs. Dysentery is the most prevalent and most fatal disease to which the colonists are subject. Few newcomers escape an attack of this malady and it carries off above one-half of the convicts who die in the Civil Hospital: the ravages of some years are much greater than others. 1788-90-91-99 and 1823 are years in which the disease was exceedingly severe and fatal. In March, 1828, a kind of hooping cough made its appearance in Sydney and spread over the whole colony. It was supposed to be introduced by the convict ship "Morely": this, however, is very doubtful and the medical profession differed much in opinion not only concerning the origin but the specific characters of the complaint. It proved fatal in a few children—the numbers were small compared to those attacked.

Consumption of the lungs, phthisis pulmonalis, is much more frequent than from the mildness of the climate might be expected and more in advanced life suffer from this disease than in England. It is remarked that in people who arrive in this colony labouring under this complaint it runs a much more rapid course than it is observed to do in colder climates.

11. *In what seasons of the year does illness most prevail and what are the seasons incidental to diseases?*

(A). Dysentery and acute diseases are most frequent in the hot weather and ophthalmia has occasionally been very troublesome in some of the districts in that season. Chronic and catarrhal infections occur in the winter. Rheumatism is common at all seasons. The Black Natives are subject to cutaneous affections from their filthy habits and peculiar mode of life.

(B). See reply to 10.

12. *What remedies do the natives employ in the diseases to which they are subject?*

(A). None that I am aware of, and it is with great difficulty that the natives can be persuaded to submit to remedies administered by European practitioners.

(B). First topical bleeding by means of a string and sometimes with a sharp quartz or a piece of broken glass: with the two latter substances the natives are known to open a vein: frequent ablutions, exposure to the air, great abstinence, friction, heat to the feet, and a long unmeaning process of superstitious incantations which commonly attends any of the above operations. In a species of Parrigo to which the natives are subject, nothing like which has yet been described, fat or any kind of grease is applied, but with what specific object I have not been able to find out. It has been asserted by many practitioners in the colony that the diseased head of the aborigines is contagious and that various children in the colony and especially in the female orphan institutions have taken the disease from them. I cannot give an opinion regarding the contagious character of the disease of the aborigines, but from a vast variety of circumstances I should strongly doubt if any adult native would be infected by ordinary communion with each other and I further think that it would be extremely difficult to infect a healthy European. This disease appears in some cases to have spread over the body, and in such a state of the disease it has never come to my knowledge that any means have been resorted to by them to effect a cure. When a native is bitten by a snake a ligature is placed above the puncture and one of the tribe snicks the wound whilst another rubs the part above it. Immersion in salt water is always practised in such cases whenever it is practicable.

13. *What is the education of those who practise medicine?*

(A). There are several individuals in the colony who have been educated in the Medical Schools of London, Edinburgh

[1] From the original in the Mitchell Library, Sydney.

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and Dublin and many others who have not received any regular professional instruction.

(B). I do not know all the gentlemen practising in the colony sufficiently well to answer the question, but there are some with whom I am acquainted whose education is of a very superior character.

14. *Have the natives any writing or tradition on medical subjects?*

(A). None.

(B). None.

15. *What is the chief diet of the natives?*

(A). On the coast their diet is chiefly fish and animal food in the interior. Vegetables are seldom used by the natives when other food can be procured.

(B). Animal food of every kind they can catch. Vegetables rarely taken except in cases of extreme hunger. The chief vegetable they use is the root of the fern.

16. *Do they practise vaccination? If so, where do they obtain lymph?*

(A). No.

(B). No aboriginal native has ever been subjected to vaccination. Vaccine lymph has been several times introduced from the Mauritius, but it has always been lost from the prejudices of the colonists in bringing forward their children and from there being no institution for the express purpose of propagating it. Lymph sent from England has never once succeeded. Several native born youths who were supposed to have been vaccinated successfully in the colony were attacked with smallpox soon after their arrival in Europe.

Correspondence.

THE USE OF PARALDEHYDE IN ALCOHOLIC DELIRIUM TREMENS.

SIR: After many years of the use of paraldehyde and other sedatives in the treatment of alcoholic *delirium tremens* I abandoned their use three years ago. The treatment of the malnutrition present and the necessity for good nursing mentioned by Professor Dawson and Dr. Cade in their letters (M. J. AUSTRALIA, August 15, 1953) must be a *sine qua non*.

I am not convinced that the restlessness of many alcoholics is due entirely to their alcoholism, for many patients suffering from the various forms of delirium, including alcoholic *delirium tremens*, have already been over-sedated by paraldehyde, bromides, chloral hydrate, morphine, hyoscine or similar preparations before admission to hospital. Further sedation only increases their restlessness. The withholding of all sedation then becomes the only common-sense treatment, which gives excellent results.

For years I had noticed that the more paraldehyde many alcoholics were given, the more restless they became. Many members of Alcoholics Anonymous, including medical practitioners, insist that during their attacks of acute alcoholism they craved for paraldehyde, because it was the only sedative that gave them a "lift". Their restlessness and tantrums whilst in hospital were deliberately designed to get further doses. I do know that when the patients are certain they will not be given paraldehyde, their tantrums cease.

My treatment of *delirium tremens* (M. J. AUSTRALIA, 1952, 2: 254) has been based on the experience gained by treating some hundreds of alcoholics in Hydebrae Private Hospital, Strathfield, during the past three years. Many of those admitted had very acute *delirium tremens*. Only three deaths have occurred, two from hepatic failure in chronic patients and one from convulsions a few hours after admission.

My experience is that death during the acute phases of alcoholic *delirium tremens* is rare. Sudden deaths do occur amongst patients after their discharge from hospital, but generally only if they keep on drinking. No cases of Wernicke's encephalopathy occurred at Hydebrae.

It is my opinion that many of the complications met with in alcoholic *delirium tremens* are due to the sedatives used in the treatment and also to the methods of nursing. The delirium caused by alcohol is in essence no different from that caused by any other toxin. Its treatment by sedatives only increases the toxæmia already present. Morphine and hyoscine, used separately, as Professor Dawson states, are dangerous, and I have never used them as such. The combination of hyoscine, morphine and atropine is effective, but its use is empirical and apparently contradictory to what I have already written.

In nursing these patients one must always remember that they are in a state of terror from their hallucinations, and in confined, closed rooms, or left alone in a restriction sheet, their terror becomes so great that they may die from heart disease. But if they are allowed to roam at will in a ward or if they are nursed in an open dormitory, where others are present, they feel themselves protected and secure, and lose their terror. This has been the experience at Hydebrae, where there are no locked doors or barred windows. At Saint Elizabeth's Hospital, United States of America, over 5000 acute alcoholics have been successfully treated under general hospital conditions during the past fifteen years. Other American hospitals have since followed this example. The same could be done in Australia, if only we could overcome our prejudices against alcoholics.

Alcoholism has become a medical rather than a psychiatric problem. Since the advent of Alcoholics Anonymous its treatment is by no means hopeless. *Delirium tremens* in itself is no longer dangerous. But the sooner we abandon the use of paraldehyde and other sedatives and shock treatment in its treatment, the sooner will we realize how quickly the patients return to mental normality. Then will we begin to appreciate the many medical problems presented by the patients, and how desperate their need for treatment. Why such a rich field for medical research has for so long been neglected is beyond my comprehension. Our prejudices against alcoholics seem to have overcome our clinical acumen.

Yours, etc.,

S. J. MINOGUE.

195 Macquarie Street,
Sydney,
August 27, 1953.

CARDIAC ARREST AS A SURGICAL EMERGENCY.

SIR: In answer to Mr. Stonham's letter on the subject of cardiac arrest, I consider the alternative plan of management suggested by him to be unsound for the following reasons:

1. If a successful outcome is to be expected when faced with this emergency, speed, the immediate institution of an adequate circulation by intermittent manual compression of the heart, and aeration of the lungs are necessary. The one essential is a knife, and anything which detracts from quick simple action is to be deprecated.

2. In a review of 1200 cases of cardiac arrest no patient who was resuscitated died of subsequent infection, so that valuable seconds must not be lost in paying "lip service" to asepsis.

3. Despite the theoretical advantages of aiding the venous return by postural means, practical experience in the reported successful cases does not bear out the necessity for these manipulations. A systolic blood pressure of 80 millimetres of mercury can be maintained manually, and experience with hypotensive anæsthetic techniques would suggest that the venous return should be adequate. There is no evidence, therefore, that these manœuvres are essential, and they may add confusion to a situation demanding quick simple action. Further, to lower the head and keep the body horizontal may obstruct the airway.

4. The opening of the pleural cavity in this particular emergency is an advantage, and not a disadvantage as suggested. The heart can be reached in a matter of seconds, often with one bold incision through the left fourth intercostal space. After the circulation has been started again the ribs can be retracted (if necessary by an assistant's hands), the pericardium opened, the heart inspected, the aorta compressed to divert blood to the brain, and if ventricular fibrillation occurs an open thorax is necessary if a defibrillator is available to be used. In actual practice these elaborate steps are rarely needed, as the heart usually starts beating again if a manual circulation is initiated soon enough. As it is essential to inflate the lungs by some means (even by mouth-to-mouth insufflation if nothing better is possible), there is no analogy between this situation and an open sucking pneumothorax.

5. The reported cases of cardiac arrest do not support the contention that the transabdominal, transdiaphragmatic approach to the heart is as good as the transthoracic one. I have tried this method on the cadaver only, but I consider it to be difficult and potentially dangerous. The difficulties are the inaccessibility of the diaphragm under the costal margin, the proximity of the left lobe of the liver and the fact that, unless special efforts are made to obtain good retraction, the incision through the diaphragm into the pericardial cavity is made blindly. The dangers are possible damage to the liver or coronary vessels. One cannot but be impressed by

the fact that so few cases have been managed successfully by the method of approach advocated by Mr. Stonham.

The term "cardiac massage", although hallowed by time, is most inappropriate when the correct measures are applied to a case of cardiac arrest. Precise and accurate expression is essential for clear thinking, and it is not undue preoccupation with semantics to hope that someone will devise a more suitable term.

There is good evidence to suggest that the complication of cardiac arrest has been increasing in recent years, and this may be one price to be paid for the remarkable advances in anæsthesia. It may occur in the most competent hands, and in the young and relatively fit. Despite the hundreds of patients who have been successfully resuscitated, the management of this condition is frequently deplorably tardy and inadequate. There will be few recoveries if indecision and timidity govern the actions of those faced with this emergency. The accumulated experiences of recent years would suggest that formal instruction in the management of this condition should be given, and in the future failure to deal adequately with this emergency may render a man liable to censure.

Yours, etc.,

135 Macquarie Street, Sydney, August 29, 1953. IAN MONK.

Reference.

STEPHENSON, H. E., REID, L. C., and HINTON, J. W. (1953), "Some Common Denominators in 1200 Cases of Cardiac Arrest", *Ann. Surg.*, 137: 731.

THYROIDECTOMY FOLLOW-UP.

SIR: Dr. Tofler has contributed a valuable study of 251 thyroidectomies done in a provincial centre. To have interviewed 171 of the patients and collated the findings is a useful piece of clinical research.

Such follow-up studies after surgery are all too infrequent; they are invariably illuminating and often salutary. Unfortunately they nearly always come from some clinic where there is a special interest and high standard in one or other branch of surgery. Excellent results are obtained and published with justifiable pride. But the uncritical reader undoubtedly gets too bright an impression of the over-all picture following the particular surgical procedure. Dr. Tofler has had the courage to show us the dark end of the thyroidectomy spectrum. But just how dark it is we cannot say. If he had told us the distribution of his 251 cases with respect to the introduction of thio-therapy in 1943 we could have judged better. It would also have helped the reader if more of the terms used had been defined. What, we may ask, does the expression "familial exophthalmos" mean? Again, the sole reason for thyroidectomy in 24 patients was "thyroid swelling", and in 16 of these (66%) the swelling was the same or worse five years later. Such frequency and extent of thyroid regeneration are, even in the present context, almost incredible. Has there been some misunderstanding?

Yours, etc.,

135 Macquarie Street, Sydney, September 1, 1953. F. F. RUNDLE.

EARLY DIAGNOSIS OF CERVICAL CARCINOMA WITH SPECIAL REFERENCE TO GENERAL PRACTICE.

SIR: In apologizing to Dr. Craig for my misinformation regarding cancer detection clinics, I must also apologize to and congratulate the Minister for Health, Dr. Turnbull, because these centres do show progress in cancer investigation, and follow along lines which have produced such excellent cancer results in Switzerland and Scandinavia.

Dr. Turnbull has had the vision to adopt this community health spirit and I thank Dr. Craig for pointing this out.

Yours, etc.,

R. F. MATTERS, Honorary Gynæcologist, Royal Adelaide Hospital.

Harley Chambers, 63 Palmer Place, North Adelaide. August 21, 1953.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED AUGUST 8, 1953.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	4(4)	..	..	1	..	..	..	5
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	15(1)	..	..	..	1	..	16
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	1	..	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	1(1)	1(1)	..	1(1)	2	1	..	6
Diphtheria	6(6)	3	5(3)	..	8(7)	..	..	..	22
Dysentery (Bacillary)	..	3(3)	..	..	..	..	..	..	3
Encephalitis	1	..	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1	..	..	..	..	..	..	1
Infective Hepatitis	..	10(7)	..	..	10(9)	..	1	..	21
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	1	..	1	..	1	..	3
Leptospirosis	..	..	4	..	..	..	..	..	4
Malaria	..	..	..	..	4(4)	..	..	..	4
Meningococcal Infection	4(1)	1(1)	2	..	..	..	..	..	7
Ophthalmia	..	..	..	..	4	..	..	..	4
Ornithosis	..	1(1)	..	..	..	..	..	..	1
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	13(10)	2(1)	2	6(4)	..	..	..	..	23
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	19(9)	1(1)	..	37(32)	..	..	..	57
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	11(6)	35(26)	3(3)	2	3(2)	1	..	..	55
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	46(37)	18(15)	52(44)	2(2)	7(4)	10(2)	..	..	135
Typhoid Fever	9(3)	1	1	..	..	..	..	2	13
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

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Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Lecture on Medical Statistics.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that Dr. H. O. Lancaster, of the School of Public Health and Tropical Medicine, Sydney, will deliver the presidential address to the Statistical Society of New South Wales, on "The Statistics of Deaf-mutism", on Thursday, October 22, 1953, at 7.45 p.m. The address will be given at the School of Public Health and Tropical Medicine. Visitors will be welcome.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 50, of August 20, 1953.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force: Medical Branch.

The probationary appointment of the following Flight Lieutenants is confirmed:—L. K. Rasmussen (025614), W. J. Ferguson (025643).

The resignation of Squadron Leader R. D. G. Vann (024187) is accepted, 22nd July, 1953.

Air Force Reserve: Medical Branch.

The following former officer is appointed to a commission 23rd May, 1953, with the rank of Flight Lieutenant:—J. Q. McCubbin (036120).

The following are appointed to commissions with rank as indicated:—(Flight Lieutenant (Temporary Squadron Leader)) John Lindsay Taylor, M.C. (297544) 23rd April, 1953, Thomas Le Gay Brereton (268020) 19th May, 1953, Thomas William Anderson (268019) 21st May, 1953; (Flight Lieutenant) Francis Xavier Morris Willis (438633) 21st April, 1953.

The following Flight Lieutenants are promoted to the temporary rank of Squadron Leader: J. P. Fleming (263942), K. J. Fagan (268007) 12th May, 1953, B. S. Mackie (268006) 3rd June, 1953.

The appointment of Flight Lieutenant W. G. Edwards (1712) is terminated 13th February, 1953.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Porritt, John Arnold, M.R.C.S. (Eng.), L.R.C.P. (Lond.), 1950, 11 Jamieson Avenue, Fairlight, New South Wales.

Haynes, Elva Grace, M.B., B.S., 1946 (Univ. Sydney), 129 Hopetoun Avenue, Vaucluse, New South Wales.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following have been registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1950: Genzel, Juliusz; Kramer, Edith Marie; Warhaftig, Hirsh George; Harmelin, Elkan.

The following additional qualifications have been registered: Cuningham, Kathleen (M.B., Ch.M., 1921, Univ. Sydney), M.S., 1939 (Univ. Sydney), F.R.A.C.S., 1939; McCullagh, Stanley Forster (M.B., B.S., 1953, Univ. Sydney), B.Sc. (Med.), 1950, Univ. Sydney; Blackman, John Edward (M.B., B.S., 1946, Univ. Sydney), F.R.C.S. (England), 1952.

Deaths.

THE following deaths have been announced:

COLE.—John Bazil Cole, on August 23, 1953, at Perth, Western Australia.

FREEMAN.—Jessie Strahorn Freeman, on August 25, 1953, at Haberfield, New South Wales.

MCLELLAND.—Hugh Sylvester McLelland, on August 29, 1953, at Brisbane, Queensland.

Diary for the Month.

SEPT. 14.—Victorian Branch, B.M.A.: Finance Subcommittee.
SEPT. 15.—New South Wales Branch, B.M.A.: Medical Politics Committee.
SEPT. 16.—Western Australian Branch, B.M.A.: General Meeting.
SEPT. 16.—Victorian Branch, B.M.A.: Clinical Meeting.
SEPT. 17.—Victorian Branch, B.M.A.: Executive of Branch Council.
SEPT. 17.—New South Wales Branch, B.M.A.: Clinical Meeting.
SEPT. 22.—New South Wales Branch, B.M.A.: Ethics Committee.
SEPT. 23.—Victorian Branch, B.M.A.: Branch Council.
SEPT. 24.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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